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IRRITABLE COLON AND GALLBLADDER DISEASE

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In an effort to determine the relation between demonstrable disease of the biliary tract and persistent symptoms of colonic dysfunction, the records of 300 patients were reviewed. The group consisted of 294 patients in whom gallbladder disease was found at operation and 6 in whom it was demonstrated at autopsy. The predominant symptom was abdominal pain. It was located in the right upper quadrant in 81, radiated to the back in 25, and extended to the right shoulder in 10. It was true biliary colic in only 156 cases. Thirteen patients were asymptomatic. There were 140 patients with multiple gastrointestinal symptoms characteristic of irritable colon. The evidence is interpreted to mean that the postcholecystectomy syndrome and related disorders are frequently part of the irritable colon problem and that good results cannot be expected from surgery unless it is supplemented by dietary measures.

THE irritable colon is an extremely common medical disorder; patients with this condition are seen by nearly every physician, whether he is in general practice or one of the various specialties. This disorder is present in about 50 to 80% of the patients seen by gastroenterologists. With the increasing stress and strain of daily living, it will undoubtedly continue to be a prominent source of annoyance and disability. Irritable colon may be defined as spasm of the large intestine, although it may also be accompanied by spasm of the small intestine. The spastic area may be large, small, single, multiple, temporary, persistent, stationary, hyperperistaltic, mild, or severe.

The problem of irritable colon has been recognized for many years and has been labeled spastic colon, spastic colitis, mucous colitis, irritable bowel, unstable colon, functional indigestion, nervous indigestion, adaptive colitis, and functional esophagogastroenterocolonopathy.[1] The variety of names applied is evidence that no single term aptly describes the multiple aspects of the disorder. Clinically and physiologically it can be further classified with related problems such as globus hystericus, cardiospasm, pylorospasm, anal spasm, and spasm of the biliary tract. Although our major objective is to present a clinical appraisal of the association of the irritable colon with gallbladder disease, we should first like to discuss a few facts and opinions about the irritable colon.

Etiology

Physiological evidence indicates that irritability of the colon results from an imbalance between the sympathetic and parasympathetic nervous control of motility in the gastrointestinal tract. Excellent

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toms persisted, and poor if the original symptoms continued or became more severe. Our findings indicate that patients with gallbladder disease may be generally classified in three groups.

Asymptomatic.—Thirteen asymptomatic patients remain well symptomatically with or without a postoperative dietary regimen, at the time of writing.

Biliary Colic.—There were 107 patients with recurrent or single attacks of biliary colic as the sole symptom. Surgical treatment is required for relief, but patients in this group remain well with or without dietary management (table 4) at the time of writing.

Irritable Colon and Gallbladder Disease.—There were 140 patients with irritable colon and gallbladder disease who experienced multiple gastrointestinal symptoms—flatus, bloating, belching, and intestinal dysfunction—with or without episodes of colic. Most remain well after operation if they continue to follow our dietary program for long or indefinite periods of time (table 4). This group also includes those patients with the most prominent psychological disturbances who are most likely to experience persistent gastrointestinal symptoms in spite of adherence to the dietary routine (table 4). Even these patients may improve with careful dietary management, however, especially under hospital control. We believe that the patients who have been classified by many observers as having biliary dyskinesia, postcholecystectomy syndrome, or chronic appendicitis also belong in this group.

TABLE 4.—*Relation of Results to Nervous Symptoms*

	Patients with Few or No Nervous Symptoms				Patients with Prominent Nervous Symptoms			
	Good	Fair	Poor	Total	Good	Fair	Poor	Total
Colic only								
On bowel management	39	0	0	39	4	0	0	4
Not on bowel management	63	0	0	63	1	0	0	1
Irritable colon with or without colic								
On bowel management	69	17	3	89	8	10	17	35
Not on bowel management	16	2	2	20	1	0	5	6

These patients may feel miserable and in many cases tend to shop from one doctor or clinic to another to obtain relief. Many refuse to accept the functional origin of the ailment and lack the insight necessary to accept the situation and make the necessary adjustment. Unfortunately, psychiatric help is also likely to be of little benefit in such instances.

The patient who complains of abdominal pain in the right upper quadrant and has a history of gallbladder operation is naturally suspected of having a common duct stone or common duct disease when seen for the first time by another physician. It is not always possible to obtain details about this previous surgery, but in many cases the removed gallbladder was normal and contained no stones. In any event, patients have often been referred to us for further common duct surgery because of recurrent right upper quadrant pain and we have been unable to find any pathological basis for the pain. The diagnosis of biliary dyskinesia is often made in these cases. Since the typical symptoms of an irritable colon are usually present, we believe the irritable colon is the underlying cause of the presenting symptoms and prefer this diagnosis. The following report describes one of the more severe cases.

Report of a Case

A 51-year-old woman was first admitted to the clinic on July 8, 1954, complaining of anorexia, postprandial distress in the right upper quadrant, substernal burning, and chest discomfort of six months' duration. She also noted a 20-lb. (9-kg.) weight loss in one year. Previous to admission to the clinic she had undergone four major surgical procedures, including appendectomy, excision of an ovarian cyst, lysis of abdominal adhesions and hysterectomy, and exploration of the left kidney. She has remained under medical care to the time of writing and has continued to experience recurring and severe episodes of abdominal pain in the right upper quadrant, abdominal cramps, nausea, vomiting, episodes of diarrhea, anorexia, and inability to gain weight. The attacks are often acute, requiring hypodermic injection for relief. Since July, 1954, she has been hospitalized on seven occasions for observation and dietary management, with temporary relief in each instance. In addition to these seven hospital stays she has undergone five more abdominal operations for the right upper quadrant pain, including laparotomy and removal of a Meckel's diverticulum, subtotal gastrectomy and gastrojejunostomy, another abdominal exploration, cholecystectomy and choledochostomy with dilation of the sphincter of Oddi, and the last operation, on Feb. 14, 1957, was another exploratory laparotomy. At that time, choledochostomy and transduodenal sphincterotomy were again performed.

No actual cause of the acute episodes of pain could be found during any of these surgical procedures. No abnormality of the pancreas or the common duct has been demonstrated after repeated examinations, and pathologically the gallbladder was normal. In fact, no organic disease has ever been discovered except for the Meckel's diverticulum, which obviously was not causing the problem. Moreover, repeated roentgenologic studies, including upper and lower gastrointestinal series and intravenous pyelograms, did not reveal any abnormality. Analysis of urinary porphyrins, urinalysis, liver function tests, pancreatic function tests, gastric analysis, and examination of feces in October, 1958, revealed no abnormality. Follow-up treatment including administration of tranquilizers and antispasmodics, dietary management, sedation, and rest has been continued, but the distress has persisted despite these measures. She has denied emotional trauma and tension throughout the years, but it is obvious that many such elements have been present, and that she has a severe general type of neurosis. She has most violently refused to be seen by any psychiatrist, despite diplomatic maneuvering on our part. It is known from another source that she has many causes for emotional disturbance.

The recent availability of intravenous cholangiography has been most helpful in ruling out the possibility of common duct stones, stricture, amputations, and retained cystic stumps containing gallstones. We carefully reviewed the histories in nine typical cases previously reported by McDonough and Wise.[7] The results of all studies, including intravenous cholangiography, were normal, as were those in the case reported. A final diagnosis of irritable colon was made, and the patients were placed on bowel management programs, with benefit.

Treatment

On the basis of the collective experience of our group in the management of thousands of irritable colon problems each year and, more specifically, after reviewing the records of the 300 patients in this series, we believe the conditions that have been termed postcholecystectomy syndrome, chronic appendicitis, and biliary dyskinesia are actually part of the irritable colon problem.[8] The facts that typical right upper quadrant pain may be produced by enema administration and that actual spasm can be demonstrated fluoroscopically in the hepatic flexure area at this time are evidence that the pain originates in the colon and not in the biliary tract. Hyperventilation seems to help relieve the spasm, and the pain may immediately disappear.

Our treatment consists of a bland diet from which obviously offending foods, fried foods, roughage, greasy foods, and spicy foods are eliminated. We further instruct our patients regarding good eating habits and recommend dental treatment, if necessary, for proper dentition and adequate mastication. They are advised to rest at least 15 minutes after meals. Laxatives and enemas are completely avoided. Oil retention enemas are allowed at bedtime to prevent rectal impactions in cases of severe constipation. Antispasmodics (especially tincture of belladonna, tridihexethyl [Pathilon] chloride, or dicyclomine [Bentyl] hydrochloride), and a mild sedative (¼ to ½ grain [15 to 32 mg.] of phenobarbital) are also prescribed before meals and at bedtime. Tranquilizers may be given for a short time in the severe cases. Heat to the abdomen (including flaxseed poultices) is advised when pain is severe. For constipation, cooked fruits two to three times daily and orange juice mixed half-and-half with hot water before breakfast are helpful. An important part of our program is the administration of hot water, six to eight cups throughout the day. This increases fluid intake and apparently has an antispasmodic effect. The patients are educated regarding normal or average bowel habits and any special aspects of the individual case are explained. The most resistant patients may require strict management in the hospital for one to two weeks in order to relieve the pain and reinstitute normal bowel function. Under the hospital regimen we have allowed patients to go as long as 100 days without a bowel movement without ill-effect. For those patients who have emotional problems whom we are unable to help, we recommend psychiatric guidance as well. Some patients still fail to respond to our program, but these are the minority. The attention and kindness of the physician are most helpful to patients with this disorder.

Summary

Patients with the irritable colon syndrome require careful treatment. By reviewing the records of 300 patients, 299 of whom had proved gallbladder disease, and presenting the statistics, we have tried to show, if not prove, that in the absence of obvious residual biliary disease, recurring pain in the right upper quadrant after cholecystectomy is caused by an accompanying irritable colon problem. Surgical treatment alone, without a dietary regimen, will only result in a large number of postoperative failures.

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Dr. Sara M. Jordan assisted in the preparation of this report.

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CLINICAL APPLICATION OF LARGE-SCALE ELECTRONIC DATA PROCESSING APPARATUS

I. NEW CONCEPTS IN CLINICAL USE OF THE ELECTRONIC DIGITAL COMPUTER

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The uses and advantages of a digital computer system in medical research were explored in a pilot study of 138 records from an outpatient clinic. Information was coded with the help of the Standard Nomenclature of Diseases and Operations, the Cornell Medical Index, and other aids, and it was found possible to punch a history of 195 questions on International Business Machine cards in 40 seconds. Manual punching can be avoided by a procedure (mark-sensing) whereby information recorded on blanks by electrographic lead pencils can be transferred directly to punch cards by machine. Data in this form can be stored easily and retrieved quickly. The study demonstrated the possibility of locating rapidly, in a very large collection of records, a group of charts meeting any desired combination of requirements.

During the last decade there has been increasing awareness of the need for improved techniques in handling clinical and research data. The increasing quantity of medical data has presented increased difficulties in the classification, search, correlation, and storage.[1] Recent developments in the field of electronic data processing and computing apparatus have indicated that there are unlimited potentialities for the adaptation of such apparatus and techniques to this problem of clinical and investigative medicine.[2] Up to the present time the use of this type of apparatus has been limited in scope to primarily statistical, sorting, and correlation studies of a narrow focus because of the marked limitation of the quantity and type of data that could be handled.[3] With the advent of the large-scale electronic digital computer, now available to most medical schools and other medical groups, the routine use of such apparatus has become feasible as an adjunct to clinical and investigative use in the evaluation of diagnostic and therapeutic problems as well as for improved medical record storage and accessibility.[4] The purpose of this paper is to present a technique for this routine clinical application in the problems of storing, correlating, retrieving, and searching for medical information.

For a number of years many medical groups and investigators have used standard punch-card accounting and tabulating equipment to carry out data processing and computational problems which have been applied to laboratory research, statistical, and epidemiologic studies. These techniques have been limited by the quantity and type of medical data or information that could be handled and made available for the search and correlation with other data. During the summer of 1958 approximately 40 medium-sized electronic digital computers were installed at various universities as well as at the National Institutes of Health for evaluation of the use of this apparatus by the universities. In the summer of 1959 the present work was initiated at the Tulane University Medical School to determine the extent of medical use of the large-scale digital computer.

Methods and Procedures

There are two broad classes of electronic computing equipment used for processing medical data: the digital computers, which use discrete electronic impulses in varying degrees to represent numerical or alphabetical information, and the analogue computers, which utilize smoothly varying levels of electromotive force to provide an analogous representative of quantitative magnitude. A mechanical example of the digital computer is the desk calculating machine, and one of the analogue computers is the slide rule. The digital computer is superior in its capacity to manipulate vast quantities of information in a complex way, in its multiplicity of types of input and output, and in its tremendous capacity for remembering. The digital computer is complicated and requires several large pieces of equipment and special housing. The preparation of data for processing and the provision of the appropriate instructions to the machine is called programming. Programming takes some time, is complex, and requires specially trained staff personnel. The analogue computer is able

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to carry out mathematical operations easily and is also able to simulate biological and physiological mechanisms, but it is not suited to the complex handling of large quantities of data. Its input is simple, its operations are manually controlled, and the results are obtained directly by means of meters, oscilloscopes, or curve tracers. It is a small piece of equipment, to be used in the laboratory.

The present work was carried out with a medium-size International Business Machine (IBM) digital computer (IBM 650) in conjunction with supplementary data processing equipment which is located at the Tulane University Computer Center.[3] Supplementary equipment included an IBM printing card punch for recording alphabetical, numerical, and special character data on IBM cards (IBM 026); a verifier (IBM 056), used to check the accuracy of data punched into the IBM cards; a sorter (IBM 082), used to classify IBM cards into numerical or alphabetical order, and a collator (IBM 077), which is a high-speed card selector and filing machine. The latter compares two sets of cards so that they may be matched, merged, and selected and their sequence may be checked. Additional equipment included a printer (IBM 402), which prepares printed records from punched cards, and a mark-sense reproducer (IBM 514), which senses data marked on the cards with electrographic lead and converts these data to punched-hole forms on the card by controlling circuits to actuate punching mechanisms.[5]

As a pilot study a group of 138 records were used from one of the Tulane Medical School outpatient clinics, each patient's chart including practically all aspects of diagnosis coding (based on the coding in Standard Nomenclature of Diseases and Operations[6]), a complete history (Cornell Medical Index and special supplementary gynecologic history), and a physical examination including a complete gynecologic examination, a roentgenographic examination, and laboratory tests. IBM cards were first used in this evaluation to determine the value of the technique as applied to the Cornell index history. The IBM cards were first punched by card punch operators who used the patient's history as a work sheet.

With the use of newer electronic recording apparatus developed to record the Cornell Medical Index in punched cards,[7] a history of 195 questions could be punched in 40 seconds. This technique did not afford the flexibility and speed offered by the mark-sense system in recording the history, the results of the physical examination, and the laboratory data. Thus, the chart number, a code number given to a particular portion of the patient record such as the cardiac examination or urinalysis, and code numbers for the various items of the record along with the actual values or magnitude of the data were recorded on Mark-Sense cards with electrographic pencils. These cards were then used to punch out the standard IBM cards to be used.

The digital computer is a magnetic memory drum which rotates at 12,500 rpm. It will retain data stored on its surface in the form of magnetic spots and provides storage space for 20,000 digits, each digit being identified by a pattern of the magnetic spots. These are permanent and available for retrieval unless they are erased and new information is recorded. In the future this or additional data can again be stored on the magnetic drum in minutes or seconds from the card data or magnetic tape of the permanent medical record. The time it takes to locate any word varies between 0.096 and 2.4 milliseconds, depending on the technique of programming.

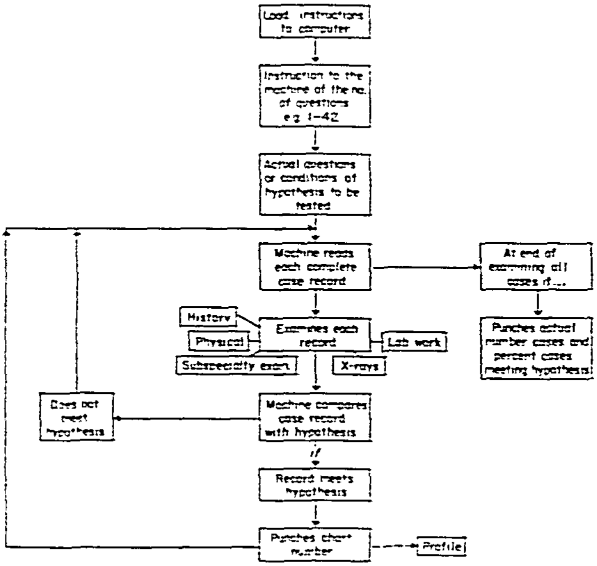
Load instructions to computer
Instruction to the machine of the no. of questions e.g. 1–42
Actual questions or conditions of hypothesis to be tested
Machine reads each complete case record
At end of examining all cases it…
History
Physical
Subspecialty exam
Examines each record
Lab work
X-rays
Punches actual number cases and percent cases meeting hypothesis
Does not meet hypothesis
Machine compares case record with hypothesis
if
Record meets hypothesis
Punches chart number
Profile

Fig. 1.—Flow of procedures of electronic digital computer evaluating clinical hypothesis.

The machine is prepared by introducing instructions on the memory drum on how to perform the problem. The control is then relinquished to the machine. The machine has to know how many questions there are in the hypothesis (of which there can be a maximum of 50), the code assigned to the finding, and the magnitude. The latter is equivalent to "greater than," "equal to," and "less than." Also included in the magnitude is information about whether the question or condition is concerned with another "or" or an "and" relationship. These instructions are given on cards to the machine for each question to be examined. After the hypothesis is fed into the machine, the patients' records are given to it. The machine examines all the records and compares each case record to the hypothesis. If the record does not agree with the hypothesis the machine skips the record and passes to the next case. If the patient's record meets the conditions of the hypothesis, it adds one case to the total group that meets the condition, punches out that case record number, and passes to the next number.

As the end of the deck of cards of patients' records is reached, there is a dummy record which shows an impossible case. When that card is reached, the computer punches out a card with the total number and percentage of patients found whose histories fulfill the conditions of the hypothesis (fig. 1). These cards are then put into the printer, which prints the hypothesis and the total number and percentage of patients found complying with the hypothesis. If the computer had been properly instructed while reading the patient records, a duplicate set of cards would have been punched for each patient found to meet the hypothesis and these cards would also have been put through the printer. This process would give a printed record of the chart numbers and a printed profile of the number of conditions met by each patient (fig. 2).

Chart Number	L lung base moist rales	R lung basal rales	L heart border over 1cm,	outside mcl	R cardiac border	enlarged	Abnormal quality	heart sounds	Aortic diastolic mur trans	Not transmitted	Aortic systolic mur	transmitted	Mitral systolic murmer	Not transmitted	Mitral systolic murmer	Not transmitted	Hepatomegaly 1cm, 2cm,	3cm, 4cm	Aortic systolic mur grade 1	Grade 2, 3, 4	Aortic diastolic mur grade 1	Grade 2,3,4	Mitral systolic mur grade 1	Grade 2,3,4	Mitral diastolic mur grade 1	Grade 2,3,4	Photoroentgenogram positive	Photoroentgenogram suggestive	Large chest x-ray positive	Large x-ray suggestive	Large x-ray–cardiac enlarge																			
98050	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
100745	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
101900	0	0	0	1	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	1	0	0	0	0	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
102120	0	0	1	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
102140	0	0	1	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
103110	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
103230	0	0	0	1	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
25290	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
48080	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
58380	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
64790	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
74520	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
83500	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
86340	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
86940	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
93790	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
101740	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
101870	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
101990	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
102000	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
102080	0	0	0	0	0	0	0	1	0	0	0	1	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
102100	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
102130	0	0	0	1	0	0	0	1	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
103020	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
103050	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
103090	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
103300	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
103360	0	0	0	0	0	0	0	0	0	0	0	0	1	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
103390	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Total cases 29 . 29

Fig. 2.—Profile of pattern of medical conditions by which specific patients have met hypothesis. Conditions of hypothesis are listed horizontally in numerical order opposite each patient's chart number, which has been presented by electronic computer. The patients meeting the hypothesis are listed by a 1 for each particular condition. A 0 has been put in to permit visual orientation. Groupings of the pattern of pathology are indicated for cardiac enlargement, types of heart murmurs, and roentgenographic findings.

Data Search and Correlation

An example of searching and correlating of data is shown by giving instructions to the computer to determine the number of cases of heart disease in the series of 138 well and asymptomatic persons. Twenty-nine patients with heart disease were noted by the machine on the basis of a history suggestive of heart disease, positive physical findings of definite heart disease, or both. These cases were detected and the record cards separated from the other patient cards.

The machine was then instructed to determine the possibility of a correlation of a number of conditions and to locate the record of a patient with all of 14 specific conditions. It was instructed to find (1) a white (2) man between (3) 40 and 49 years of age, who (4) might have known he had hypertension but who (5) did not know that he had heart disease. He had to have (6) cardiac enlargement with the left ventricle percussed over 1.0 cm. outside the midclavicular line and (7) a *pulse with a normal sinus rhythm less than 90* per minute, and (8) the second aortic sound had to be greater than the pulmonic without a heart murmur. (9) The prostate had to be firm and slightly enlarged. All of the preceding conditions had to be present, with (10) a hemoglobin level of no less than 14.0 Gm. and a urinalysis showing (11) a specific gravity over 1.020 but (12) negative results for albumin tests and with (13) glycosuria and (14) occasional pus cells on microscopic examination. It is possible to correlate up to 50 such conditions. A patient with the 14 conditions was present, and his record was given along with information about what percentage of the group he constituted.

Another technique of value is the ability to obtain visual profiles of the hypothesis being tested. Thus, in searching for the patients with heart disease, the machine also recorded the chart numbers of patients meeting the conditions as well as the conditions noted in each patient's record, which could be scanned for a pattern of the pathology or conditions being studied.

The machine was instructed to scan the 138 charts for patients with heart disease and, at the same time, to punch out a duplicate set of cards for each of the cardiac patients. These cards, which make up a smaller deck from the main group, could be further investigated. The cards were then processed through an IBM printing machine, which listed the hypothesis of 32 conditions presented to it in the original instructions and then listed the patients' chart numbers. Opposite each chart number were indicated the specific conditions through which that particular patient met the hypothesis (fig. 2). It will be noted that the 302 conditions making up the hypothesis are listed horizontally in numerical order in groups of 10 and that the positive relationships are indicated by the figure 1. The grouping of these indicates the frequency of the findings.

The technique of presenting instructions to the machine in the programming is exemplified by an example of a simple Probe to test the hypothesis that the majority of well and asymptomatic males between 30 and 50 years of age who have hypertension will exhibit cardiac or renal pathology but will be unaware of their conditions. (Probe is the name given to the technique for testing with a digital computer a complex medical hypothesis against a mass collection of clinical case data.) This hypothesis could be tested in several ways. One way would be to instruct the machine to scan the records of the 138 patients and to give the chart numbers of any with the diagnosis coded as hypertension or hypertensive cardiovascular disease in Standard Nomenclature of Diseases and Operations. This would make a smaller group of records with which to work. Actually, the problem was approached in order to use the history and physical and laboratory findings for the entire series, the machine being instructed to scan the 138 patients for 30 specific conditions in the following way:

1	000	196	9	0002	9	history	had to be over 29 years of age
2	000	196	9	0005	8	history	had to be less than 50 years of age
3	000	197	9	0004	0	history	had to be male
4	101	003	9	0150	9	physical examination	had to have systolic blood pressure of 150 or over
5	101	004	9	0100	9	physical examination	had to have diastolic blood pressure of 100 or more
6	000	028	8	0009	0	history	had been told he had high blood pressure
7	000	039	8	0009	0	history	had been told he had heart trouble
8	000	107	8	0009	0	history	had been told he had bladder or kidney disease
9	110	004	8	0000	9	urinalysis	albuminuria (trace to 4 plus)
10	110	008	8	0000	9	urinalysis	hyaline casts
11	110	010	8	0000	9	urinalysis	granular casts
12	110	011	8	0001	0	urinalysis	white blood cell count; occasional to innumerable casts
13	110	011	8	0001	9	urinalysis	white blood cell count; occasional to innumerable casts
14	110	007	8	0001	9	urinalysis	red blood cell count
15	110	006	8	0001	9	urinalysis	white blood cell count
16	102	014	8	0001	0	lungs	rales, left base
17	102	017	8	0001	0	lungs	rales, right base
18	102	039	8	0000	9	heart	left border outside midclavicular line
19	102	040	8	0000	9	heart	right ventricular enlargement
20	102	041	8	0001	0	heart	sounds, soft quality
21	102	041	8	0002	0	heart	sounds, poor quality
22	102	041	8	0003	0	heart	sounds, aortic greater than pulmonic
23	102	041	8	0004	0	heart	sounds, pulmonic greater than aortic
24	102	042	8	0000	9	heart	aortic diastolic murmur (transmission)
25	102	043	8	0000	9	heart	aortic systolic murmur (transmission)
26	102	044	8	0000	9	heart	mitral systolic murmur (transmission)
27	102	045	8	0000	9	heart	mitral diastolic murmurs (transmission)
28	202	001	8	0000	9	heart	aortic systolic murmur, grades 1-4
29	202	002	8	0000	9	heart	aortic diastolic murmur, grades 1-4
30	202	003	8	0000	9	heart	mitral systolic murmur, grades 1-4
31	202	004	9	0000	9	heart	mitral diastolic murmur, grades 1-4

It will be noted that the first column is the numerical order of the conditions of the hypothesis. The second column is the code given to the specific portion of the chart, such as the history, physical examination, or specific laboratory examination. The third column is the subdivision of the information given in the previous column. The fourth column indicates the connective "or" (designated by an 8) or "and" (designated by a 9); the fifth, the magnitude of the data in question; and the sixth, the connective "equal to" (designated by a 0), "less than" (indicated by an 8), or "more than" (indicated by a 9).

The machine then showed that 2 men complied with the conditions of the hypothesis, giving the percentage as 1.5% of the 138 patients scanned. Putting these two records through the printing machine resulted in the following profile:

```
 30190..........  1111001000  1000000000  0000000000  0000000000  0000000000
101830..........  1111111100  0000000000  0000000000  0000000000  0000000000
```

conditions of the hypothesis, it adds one case to the total group that meets the condition, punches out that case record number, and passes to the next number.

As the end of the deck of cards of patients' records is reached, there is a dummy record which shows an impossible case. When that card is reached, the computer punches out a card with the total number and percentage of patients found whose histories fulfill the conditions of the hypothesis (fig. 1). These cards are then put into the printer, which prints the hypothesis and the total number and percentage of patients found complying with the hypothesis. If the computer had been properly instructed while reading the patient records, a definite heart disease, or both. These cases were detected and the record cards separated from the other patient cards.

The machine was then instructed to determine the possibility of a correlation of a *number* of conditions and to locate the record of a patient with all of 14 specific conditions. It was instructed to find (1) a white (2) man between (3) 40 and 49 years of age, who (4) might have known he had hypertension but who (5) did not know that he had heart disease. He had to have (6) cardiac enlargement with the left ventricle percussed over 1.0 cm. outside the midclavicular line and (7) a pulse with a normal sinus rhythm less than 90 per minute, and (8) the second aortic sound had to be tasks and by which it accomplishes the probing search and correlation of data is known as Medical Probe.

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ANTIHYPERTENSIVE DRUG VERSUS SYMPTOMATIC TREATMENT IN PRIMARY HYPERTENSION

EFFECT ON SURVIVAL

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An effort was made to determine the possible role of antihypertensive drugs in lengthening the life of patients with primary hypertension. The 58 patients satisfied rigid criteria for the diagnosis of primary hypertension, and all had had it for at least five years. They were divided into two equal, matched groups, 16 of the 29 matched patient-pairs being male. The test group received a variety of antihypertensive drugs sufficient to maintain blood pressures at or below 160/104 mm. Hg. None of these drugs were given to the contratest group. Both groups received sedatives, analgesics, digitalis, and diuretics as needed and were otherwise treated alike. Within the subsequent seven-year period of observation, 16 patients in each group died, and no significant difference between the two groups was found.

It is accepted generally that antihypertensive drugs are of value in prolonging the life of at least some patients with the accelerated form of hypertension. There is agreement also that such drugs may relieve symptoms and modify some complications in many patients with primary hypertension who do not have the accelerated form. Although reports are beginning to appear in this latter group which suggest beneficial effects on survival,[1] it is not easy as yet to obtain large enough series or satisfactory yardsticks for comparison. Certainly much more time must elapse before any valid statements can be made concerning patients with early, uncomplicated disease.

The present study is another effort to determine the possible role of antihypertensive drugs in lengthening the life of patients with primary hypertension. It represents a seven-year period of observation; the technique used matches each treated subject to one who is identical in all measured parameters[2] and is receiving only symptomatic therapy.

Case Material and Methods

Twenty-nine patients and their matched controls were selected for this study. All had an established diastolic hypertension[3] known and documented for at least five years before treatment. Patients with the accelerated form of hypertension, secondary hypertension,[3] diabetes, other endocrine disorders, or valvular heart disease were excluded from both series. All were private or clinic patients who were examined and followed up at intervals of six months or more frequently by me and in interim periods by other physicians unaware of the study program. The antihypertensive drugs received by the index patients included varying doses of hexamethonium, pentolinium, or mecamylamine, generall le- mented by rauwolfia alk hydralazine as well. A

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only hydralazine and a rauwolfia alkaloid. Shifts were made occasionally from one ganglionic-blocking drug to another. All medicaments were given by mouth and their administration continued uninterruptedly until dosages were modified or treatment terminated by a complication. At no time did the matched control patients receive any of these drugs; however, most were treated at one time or another with phenobarbital or chloral hydrate and sometimes with other sedatives or mild analgesics. All patients in both groups were advised to avoid excesses of salt or were restricted to not less than 2 Gm. of sodium chloride per day. Digitalis and diuretics, such as mercurials or chlorothiazide, were used in some patients in both groups only for congestive failure.

Fate of Hypertensive Patients Treated with Antihypertensive Drugs (D) Compared with Matched Controls Treated Symptomatically (S)

			Standing Blood Pressure, Mm. Hg				Pretreatment Data†				
			Pretreatment		Post-treatment						
Case No.	Sex	Age*	Maximum	Minimum	Maximum	Minimum	Heart Enlarged	Headache	Proteinuria	Cause of Death‡	Time of Death (Post-treatment), Mo.
1D	M	52	240/150	220/120	160/100	120/84	1	1	0	CF	50
1S	M	50	290/160	210/120	280/160	180/110	1	1	0	...	..
2D	M	49	250/130	184/104	154/96	100/74	1	2	+	...	..
2S	M	50	250/130	170/100	240/150	190/110	2	1	+	MI	29
3D	M	44	240/130	180/100	160/100	90/60	2	0	0	...	..
3S	M	44	240/140	166/100	240/140	150/110	2	1	0	...	..
4D	M	52	280/160	170/100	146/96	110/80	1	2	0	CVA	12
4S	M	49	250/140	150/90	220/140	176/100	1	3	0	CF,?MI	71
5D	M	48	200/130	146/96	140/90	100/60	1	1	0	...	..
5S	M	50	240/140	160/90	220/140	150/90	0	0	0	CVA	50
6D	M	48	260/130	190/110	158/100	130/88	2	1	0	MI	32
6S	M	50	250/140	180/100	220/140	160/100	2	2	0	MI,CF	44
7D	M	46	246/125	210/110	156/100	140/90	2	0	0	...	..
7S	M	44	240/130	200/100	260/150	196/94	1	0	0	CVA	46
8D	M	49	240/140	170/100	154/104	90/60	1	2	0	MI	56
8S	M	46	264/144	180/80	270/130	170/90	0	0	0	MI	72
9D	M	46	190/150	166/114	150/100	130/90	1	0	0	CVA,CF	51
9S	M	49	230/154	160/104	220/150	180/100	1	0	0	...	..
10D	M	46	254/142	180/100	140/100	110/80	2	1	++	An	27
10S	M	47	240/130	174/104	260/140	190/120	1	0	++	CF	22
11D	M	44	240/136	200/110	150/100	100/70	1	1	0	...	..
11S	M	41	220/140	180/110	220/140	180/110	1	0	0	...	..
12D	M	48	220/140	190/106	160/100	134/94	2	1	+	CVA	19
12S	M	48	250/148	230/120	240/140	170/110	2	1	+	MI	30
13D	M	51	240/130	130/80	140/90	124/76	1	2	0	...	..
13S	M	48	230/125	126/78	240/145	140/90	0	1	0	CVA	37
14D	M	41	210/126	150/100	150/104	130/84	2	0	0	MI	80
14S	M	44	180/120	150/100	200/120	180/114	2	1	0	MI	64
15D	M	46	184/120	170/100	156/100	140/90	2	1	0	MI,CF	70
15S	M	46	190/120	166/96	200/124	170/104	2	2	0	...	..
16D	M	47	256/146	200/100	160/100	130/88	1	2	0	...	..
16S	M	50	290/158	180/110	285/150	150/100	2	2	0	...	..
17D	F	43	210/120	160/94	136/90	120/80	3	3	+	MI	26
17S	F	46	216/128	150/90	240/126	140/86	3	3	+	MI	6
18D	F	50	200/120	150/96	160/100	130/84	2	1	0	CVA	44
18S	F	47	196/126	170/90	200/100	160/94	2	1	0	...	..
19D	F	42	180/120	140/100	140/100	130/90	1	2	0	...	..
19S	F	43	210/124	156/112	200/126	150/110	1	1	0	...	..
20D	F	47	220/120	200/100	150/96	130/88	1	3	0	CVA	29
20S	F	46	220/130	130/80	200/130	140/86	1	2	0	CF	18
21D	F	48	180/120	170/110	140/100	120/80	2	0	0	MI,CF	36
21S	F	45	170/120	154/96	180/120	162/92	2	0	0	...	..
22D	F	52	250/140	200/110	160/100	140/90	1	1	0	CVA,CF	30
22S	F	52	230/140	210/126	250/150	200/100	2	0	0	...	..
23D	F	45	190/124	160/100	146/94	110/72	1	0	0	...	..
23S	F	48	186/130	160/96	200/120	150/100	1	0	0	...	..
24D	F	47	184/124	160/116	140/90	120/80	2	2	+	...	..
24S	F	46	190/130	160/110	220/140	200/120	2	2	+	MI,CF	57
25D	F	48	256/124	200/110	160/100	144/94	1	0	0	MI	30
25S	F	47	240/130	196/114	280/150	220/110	1	1	0	CF	46
26D	F	50	240/120	215/105	160/100	134/82	2	1	0	...	..
26S	F	47	250/120	200/100	280/120	200/100	2	0	0	...	..
27D	F	48	222/146	192/118	158/104	94/72	1	0	0	MI	80
27S	F	45	230/150	190/110	200/120	180/100	1	1	0	CVA	73
28D	F	46	180/120	150/90	150/100	100/70	1	1	0	...	..
28S	F	46	170/126	158/94	190/120	140/100	1	0	0	CVA	59
29D	F	41	240/140	200/124	160/100	140/90	2	2	0	...	..
29S	F	44	230/140	216/120	220/130	180/110	1	2	0	...	..

* At start of treatment period.

† 0 = not present; 1 = slight or mild; 2 = moderate; 3 = marked or severe.

‡ CF = congestive failure; MI = myocardial infarction; CVA = cerebral vascular accident; An = ruptured abdominal aortic aneurysm.

In addition to the documented diagnosis of primary hypertension of five or more years' duration, the following criteria were used arbitrarily to select the index patients to be treated with antihypertensive drugs and to maintain them in the study: age at start of treatment not less than 41 or more than 52 years; at least one casually recorded standing diastolic blood pressure of 120 mm. Hg or higher; an abnormal electrocardiogram indicative of left axis deviation and myocardial damage but not suggesting an antecedent myocardial infarction; no pretreatment history of angina pectoris, myocardial infarction, congestive failure, or cerebrovascular accident; no retinal hemorrhages, "exudates," or papilledema; no nitrogen retention; seven years of antihypertensive drug therapy during which time, after the initial response, there was no blood pressure reading in the standing position in excess of 160/104 mm. Hg as recorded by any physician; and death, if it occurred, the result of a hypertensive complication. Each of the above patients was then matched retrospectively to a patient treated symptomatically who was within three years of the same age and of similar sex and race and who had comparable standing, casually recorded blood pressures secured over at least a two-year period as a base line, and the same clinical and laboratory picture. The matched control cases, when they fulfilled these criteria, were then designated post-treatment and each course followed in parallel with its index case. Only patients whose symptomatic treatment period began after 1949 were used as controls, and the matching was done without knowledge of the clinical outcome of either the control or the index case. Sixteen of the 29 matched patient pairs were male.

Results.—Additional data, blood pressure ranges prior to complications, causes of death, and post-treatment month at which death occurred are shown in the table. Of the 32 male patients, 9 treated with antihypertensive drugs and 10 treated symptomatically have died. Of the 26 female patients, 7 treated with antihypertensive drugs and 6 treated symptomatically have died. The rest, all of whose progress has been followed for seven years, are still alive.

Thus, a total of 16 of 29 antihypertensive drug-treated patients and 16 of 29 symptomatically treated patients have died within a seven-year period of observation. The average period of survival of the drug-treated group was 42 months and that of the control group 45 months. It is evident that most deaths can be ascribed to atherosclerotic complications.

Comment

This study, dealing with the action of antihypertensive drugs as compared to symptomatic therapy in matched patients with primary hypertension, indicates that the resultant lowering of the casually recorded standing blood pressure is unassociated with a demonstrable lengthening of the life span. Before interpretations can be made from these observations, considerable qualification is required. First, it is most unlikely that blood pressures were maintained at levels of 160/104 mm. Hg or less "around the clock" or when the patients were supine. Second, it should be emphasized that this series of patients is small and that the index cases are selected. Finally, only patients with long-standing hypertension with signs of myocardial damage, generally associated with cardiac hypertrophy and sometimes with possible early nephrosclerosis, were included.

The possibility that antihypertensive measures may lengthen the survival of patients with early, uncomplicated disease; of patients with congestive failure; or of patients in other age groups cannot be gauged in any way from the present study. Nevertheless, it is suggested that the burden of proof, that drugs which lower the arterial pressure will prolong the lives of patients with primary hypertension who do not have the accelerated form of disease, must rest with those who make such claims.

Summary

Twenty-nine patients with primary hypertension, all of whom had had an elevated blood pressure for more than five years and had developed electrocardiographic signs of myocardial damage, were treated for seven subsequent years with antihypertensive drugs in dosages sufficient to produce a standing blood pressure of 160/104 mm. Hg or less. Each of these patients was matched to a hypertensive subject similar in all measured parameters but treated symptomatically. During the period of observation 16 patients in each group died, there being no significant difference in their average survival whether or not they received antihypertensive drugs.

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EFFECTS OF P-DI-(2-CHLOROETHYL)-AMINOPHENYLALANINE ON MALIGNANT TUMORS

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A group of 60 patients with far-advanced malignant tumors was selected for therapeutic trial of p-di-(2-chloroethyl)-aminophenylalanine. The drug was administered orally or by segmental perfusion usually in a dosage of 2 mg. per kilogram of body weight. Some patients showed no improvement, some improved for a time only to relapse later, but in some the improvement was lasting. The most marked improvement was in patients with sarcoma, particularly Hodgkin's disease, fibrosarcoma, Kaposi's sarcoma, and neurofibrosarcoma. Next in order of susceptibility to the drug were melanomas and carcinoma of the breast. Occasional cases of carcinoma of the lung, tongue, ovary and colon were susceptible but for shorter periods of time. Bone marrow depression in varying degrees was the side-effect, rarely observed with the oral administration, more frequently with the segmental perfusion.

In 1953 Larionov[1] synthesized p-di-(2-chloroethyl)-aminophenylalanine and demonstrated its tumor-inhibitory effects in experimental animals and in human patients. Creech and others[2] used the same agent in treating malignant tumors in human beings. However, in this instance the drug was confined within the isolated anatomic segment containing the tumor, while circulation was maintained by means of an extracorporeal circuit. Favorable effects were noted in melanomas after treatment of an extremity in this manner.

This work is concerned with a clinical trial of p-di-(2-chloroethyl)-aminophenylalanine (Sarcolysin, Sarcolysine, [nitrogen mustard]) given orally or by segmental perfusions, in advanced cases of various malignant tumors in human beings.

Method of Study

A randomized group of 60 patients with far-advanced malignant tumors was selected for therapeutic trial. These patients had failed to respond to all standard methods for the control of their tumors. Many had responded previously to other chemotherapeutic agents and were then treated with p-di-(2-chloroethyl)-aminophenylalanine. A total dose of 2 mg. per kilogram of body weight of p-di-(2-chloroethyl)-aminophenylalanine was orally administered over a four-day period as the initial course. The basic studies consisted of a complete blood cell and platelet count, serum protein, uric acid, and alkaline phosphatase determinations; and blood calcium level measurements in patients with breast carcinoma presenting osteolytic metastases. In 45 patients a minimum course of the drug (2 mg. per kilogram of body weight) was administered. The remaining patients, because of the terminal status of their disease, were unable to receive at least a full initial course of the drug. The criteria for withholding a drug or discontinuing its administration was a white blood cell count of less than 3,000 per cubic millimeter and a platelet count of less than 75,000 per cubic millimeter. Both blood elements appear to be equally effected by administration of p-di-(2-chloroethyl)-aminophenylalanine. In patients in whom favorable effects were noted, further therapy was withheld until such time as evidence of relapse became manifest. In these cases, usually 1 mg. per kilogram of body weight was administered over a two-day to four-day period, depending on the status of the marrow response.

Seven patients with localized nonresectable tumors were treated by segmental perfusion. P-di-(2-chloroethyl)-aminophenylalanine, in a dose of 2 mg. per kilogram of body weight, was added to the extracorporeal circuit, which was connected to the vascular supply of the anatomic segment containing the nonresectable tumor. The patients were heparinized with 2 mg. of heparin per kilogram of body weight. In six of these patients the tumors were in the pelvis. In these patients the connections to the extracorporeal circuit were established by placing cannulas within the inferior vena cava and the abdominal aorta distal to the origin of the inferior mesenteric artery during laparotomy. The diversion of blood from this segment to the extracorporeal circuit was then established by temporary occlusion of both the aorta and the vena cava proximal to the points of entry of the cannulas. The blood of the extracorporeal circuit was excluded from the legs by the application of

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pneumatic tourniquets to the thighs. In one patient in whom the upper extremity was perfused, cannulas were inserted in the second portion of both the axillary vein and artery. Connection to the extracorporeal circuit was established by temporary occlusion of the aforementioned vessels proximal to the point of entry of the cannulas. Prior to perfusion, the patient received 2 mg. per kilogram of body weight of heparin. Perfusion of the involved part was maintained for an average time of 16 minutes. At the conclusion of the period of perfusion the venous blood from the segment was discarded while an average of 1,000 cc. of blood was pumped into the segment by means of the extracorporeal circuit. In one patient (case 57) the segment was first flushed with 1,500 cc. of saline solution prior to the final replacement with 1 liter of blood. The cannulas were then removed from the vessels and the defects in the vessels sutured with fine silk. After the reestablishment of normal circulation to the treated areas, the heparin effect was neutralized by the intravenous administration of protamine. The amount of protamine needed to insure normal coagulation was determined by repeated measurements of the coagulation time of the patient's blood during the slow administration of protamine. Usually no more than 20 mg. of protamine was necessary for this purpose.

The extracorporeal circuit is of new design and consists of one pump, a dispersion-type oxygenator, and is completely automatic in operation. The oxygen tension within the oxygenator is 1,000 mm. Hg. (Details and performance of the extracorporeal circuit are to be published soon).

Therapy

With the exception of patients treated by perfusion, favorable objective evidence of treatment, when obtained, was noted usually within four weeks after the administration of the drug. In the former instances, objective effects were noted in four patients within two weeks. Massive necrosis was observed in two patients after perfusion with p-di-(2-chloroethyl)-aminophenylalanine and in one patient after oral administration of the drug. Other patients favorably affected exhibited gradual regression of tumor masses without ulceration.

Carcinoma of the Breast.—Seven patients with carcinoma of the breast were treated with p-di-(2-chloroethyl)-aminophenylalanine when relapse became evident after ablative or additive hormonal therapy. Five patients had also received triethylene thiophosphoramide (Thio-TEPA). Of these patients, five had had radical mastectomies originally. Repeated excisions of tumors had been performed on the sixth patient, none of which had been diagnosed as malignant. The remaining patient had had a simple mastectomy for inflammatory carcinoma of the breast, together with simultaneous ablative hormonal treatment.

In one patient (case 1), the recurrence of hoarseness due to progression of a tumor in the mediastinum subsided within three weeks after the institution of p-di-(2-chloroethyl)-aminophenylalanine therapy. In addition to the improvement in hoarseness, she has shown objective improvement, manifested by a decrease in the size of the mediastinum and no further evidence of progression of her disease. At the time of writing this remission has been maintained for nine months.

Three patients (cases 2, 3, and 4) maintained on cortisone therapy showed evidence of progression of their disease. One patient (case 2), developed a mass in the remaining breast and increasing lymph node involvement. In two patients (cases 3 and 4) this was manifested by increasing dyspnea and the appearance of osteolytic metastasis in the calvarium. These patients also had an increase in calcium excretion. In all three patients an objective remission has been maintained for four and eight months, manifested by calcification of osteolytic lesions and a decline in calcium excretion. These patients have been maintained in good condition by continuation of cortisone therapy supplemented by periodic courses of p-di-(2-chloroethyl)-aminophenylalanine when there was objective evidence of formation of new lesions or progression of old lesions. The conditions of three other patients (cases 5, 6, and 7) previously treated by the same method continued to deteriorate rapidly despite treatment with p-di-(2-chloroethyl)-aminophenylalanine.

Hodgkin's disease.—Eight patients with Hodgkin's disease involving mainly the lungs were treated with p-di-(2-chloroethyl)-aminophenylalanine. All patients had been previously treated by a combination of surgery, x-radiation, and triethylenethiophosphoramide. In two patients (cases 8 and 9) treatment was followed by a complete and persistent disappearance of all lesions from the lung, as determined by roentgenographic studies. In both patients the remission has been maintained for at least 16 months. A significant response was obtained in case 10, in which recurrent Hodgkin's disease, after excision of the primary tumor mass from the posterior mediastinum, had subsequently progressed and involved the hila of both lungs and the right pleural cavity. After therapy with p-di-(2-chloroethyl)-aminophenylalanine, the tumor masses in the hila of the lungs decreased in size. This was associated with general improvement. In one patient (case 11) there was development of an infraclavicular tumor mass which decreased to one-third its original size after treatment with p-di-(2-chloroethyl)-aminophenylalanine. One patient (case 12) with recurrent involvement of the lungs responded well for only a short time. Within two months the disease recurred and progressed rapidly. One patient (case 13) had metastatic involvement of the vertebrae, but responded to a combination of x-ray and p-di-(2-chloroethyl)-aminophenylalanine ther-

Treatment of Sixty Patients with Malignant Tumors with P-di-(2-chloroethyl)-aminophenylalanine

Malignancy, Type or Site	Case No.	Previous Treatment	Status	Dose, Mg.	Effect	Duration of Favorable Effect	Result	Hemato-logical Effect
Breast	1	Radical; oophorectomy; cortisone, triethylenethiophosphoramide; fluoxymesterone (Halotestin); x-ray	Recurrent hoarseness	100	Subsidence of hoarseness and marked general improvement	9 mo.	Living	None
	2	Radical; x-ray; laminectomy; cortisone	General deterioration	80	Improved	8 mo.	Living	None
	3	Oophorectomy; cortisone; triethylenethiophosphoramide	Maintained remission with slightly enlarging mass in left breast	100	Decrease in size of breast mass; general improvement	4 mo.	Living, improved	None
	4	Radical; androgen; cortisone; triethylenethiophosphoramide	More dyspneic	80	General improvement	8 mo.	Living, improved	Slight
	5	Radical; triethylenethiophosphoramide, cortisone; radiation	Rapidly progressive	160	No improvement		Died	Moderate
	6	Simple mastectomy; oophorectomy; cortisone, triethylenethiophosphoramide	Progressive	320	No improvement		Died	Marked
	7	Radical; cortisone; androgen	Progressive bone involvement	320	No improvement		Died	Slight
Hodgkin's disease	8	Local surgery	Pulmonary metastasis	100	Excellent	16 mo.	Living	None
	9	Biopsy, x-ray	Pulmonary metastasis	120	Excellent	10 mo.	Living	None
	10	Excision primary tumor; HN_2, x-ray	Pulmonary metastasis; pleural fluid	100	Marked regression of pleural metastasis	5 mo.	Living, improved	Slight
	11	Excision of involved nodes; x-ray; nitrogen mustard	Nodes left supraclavicular fossa	120	Regression	2 mo.	Living, received nitrogen mustard again	Slight
	12	Surgery (lobectomy); cobalt, triethylenethiophosphoramide	Widening of mediastinum	200	Maintained decrease in size of mediastinum	2 mo.	Died	Moderate
	13	X-ray	Lesion in vertebrae	100	Regression; no new lesions	6 mo.	Living	None
	14	ACTH, x-ray	Diffuse adenopathy; lung lesion	100	Marked regression	3 mo.	Living, improved	None
	15	None	Diffuse adenopathy; hepatic enlargement	100	Complete regression	3 mo.	Living, improved	None
Lung	16	Thoracotomy	Pleural involvement	220	General improvement	11 mo.	Living	None
	17	Thoracotomy	Progressive	80	General improvement; absence further progression	5 mo.	Living	Slight
	18	ACTH, triethylenethiophosphoramide, chlorambucil, x-ray	Recurrent mediastinal mass	100	Slight regression	5½ mo.	Died	Mild
(Pleural (metastatic; primary not known))	19	Rapid progression	Pulmonary metastasis	320	Improved control of fluid	1½ mo.	Died	None
Ovary	20	Exploration and biopsy	Huge ascites	120	Slight, if any	3 wk.	Died	None
	21	Biopsy	Masses	280	Improved	4 mo.	Died	None
	22	Biopsy	Masses; fluid	210	Improved	3 mo.	Died	Moderate
	23	None	Progressive	60	None		Died	Moderate
	24	Surgery, x-ray	Recurrent tumor masses; ascites	80	Marked disappearance of fluid and masses	1½ yr.	Died of intestinal obstruction due to fibrosis	None
Endometrium	25	X-ray; triethylenethiophosphoramide	Rapidly progressive	110	None		Died	None
Uterus, fibrosarcoma	26	Surgery, excision two times	Postoperative	210	Remains static	8 mo.	Recurrent, where before had recurrence in 2 months	None
Tongue	27	Surgery, radiation	Progression	320	Decrease in size	1 mo.	Died inanition	None
	28	Radiation	Progression	100	Decrease in size	Unknown	Lost to follow-up	Severe
	29	Surgery; radiation	Ulceration	80	Decrease in size	1 mo.	Died inanition	Mild
Melanoma	30	Treated by quack with enemas	Huge axillary tumor mass	200	Complete necrosis		Died from protein loss (needed removal of necrotic mass)	Slight
	31	Excision primary tumor	Apparently completely excised	150	No recurrence	9 mo.	Living	None
	32	ACTH	Multiple skin lesions; possible CNS lesion	80	None		Living	None
Neurilemmoma	33	Surgery, x-ray	Rapidly progressive	200	Slight improvement in some lesions; marked in lesion in thigh	2 mo.	Died	Slight
Fibrosarcoma	34	Surgery, incomplete excision	Inoperable	200	Maintained remission, disappearance residual masses	8 mo.	Remission (excellent)	None
Kaposi's sarcoma	35	Biopsy numerous nodes	Disseminated; psoriasis	100 (dexamethasone)	Complete regression	9 mo.	Living and well	None

Treatment of Sixty Patients with Malignant Tumors with P-di-(2-chloroethyl)-aminophenylalanine—Continued

Malignancy, Type or Site	Case No.	Previous Treatment	Status	Dose, Mg.	Effect	Duration of Favorable Effect	Result	Hematological Effect
Colon	36	Resection; chloropactin in operative field; triethylenethiophosphoramide, 200 mg.	Recurrent	160	General improvement, enlargement of tumor mass due to hemorrhage and necrosis	6 mo.	Improved—patient reoperated; died	Slight
	37	Surgery	Recurrent	160	Excellent remission, disappearance of tumor masses	3 mo.	Relapse with progression	None
	38	Surgery	Disseminated	150	None detectable		Progressive—died	Slight
	39	Resection; triethylenethiophosphoramide	Recurrent	160	None detectable		Progressive—died	Moderate
	40	Resection; triethylenethiophosphoramide	Recurrent	30	None		Died	Moderate
	41	Resection	Recurrent	220	None		Progressive—died	Moderate
	42	Resection; triethylenethiophosphoramide, 600 mg.	Recurrent	200	None		Progressive—died	None
	43	Resection; triethylenethiophosphoramide	Recurrent	220	None		Progressive—died	Slight
	44	Surgery; triethylenethiophosphoramide, Methotrexate	Recurrent	310	Necrosis and some decrease in size	4 mo.	Short regression, then progression—died	None
Stomach	45	Triethylenethiophosphoramide, 100 mg. intraperitoneally	Rapidly progressive	80	None		Died	None
Lymphoepithelioma	46	Lung decortication; local mustard, triethylenethiophosphoramide	Progressive	80	None		Died	
Wilms's tumor	47	Nitrogen mustard	Pulmonary metastasis	30	None		Living—responded to actinomycin therapy	Slight
Osteogenic sarcoma	48	None	Rapidly progressive	60 oral 30 I.V.	None		Died	Slight
Mucoid adenocarcinoma	49	Radiation	Diffuse abdominal masses	300	None		Died	None
Neurofibrosarcoma	50	Surgery; incomplete excision	Inoperable	320	Maintained remission	11 mo.	Remission	None
Prostate	51	Orchiectomy and estrogens	Progressive	200	None		Died	None
Malignant lymphoma	52	Radiation; nitrogen mustard 3 times; CH3, nitrogen mustard	Disseminating	220	Slight regression	1 mo.	Died	Slight
Larynx	53	Surgery; x-ray	Local extension	240	Questionable	1 mo.	Died	None
CASES TREATED by Perfusion with P-di-(2-chloroethyl)-aminophenylalanine								
Urethra	54	Surgery; x-ray	Rapidly locally progressive	160 oral 150 Perfusion	Recurrent, patient perfused	9 mo.	Living	None
Melanoma	55	Local excision 6 times	No evidence recurrence	30 11 min. Perfusion	Softening of area	6 mo.	Living	None
Bladder	56	Radium; x-ray	Enlarging left inguinal mass; edema leg	160 Perfusion	Necrosis, relief of pain	1 wk.	Died	Profound effect
	57	Surgery; radiation	Progressive	150 Perfusion	Necrosis	13 day	Died	Severe
	58	Surgery; radiation	Progressive	120 Perfusion	Necrosis	6 wk.	Died	None
Colon	59	Mile's resection	Perineal recurrence	120 Perfusion	Disappearance of tumor mass followed by recurrence on side opposite perfused area	4 mo.	Recurrent	None
	60	Resection and anastamosis	Recurrent mass in abdominal wall	56 Perfusion	Partial regression	8 wk.	Improved—regression	None

apy. The remission has been maintained for six months (at the time of this writing), with no new evidence of the disease. Two patients (cases 14 and 15) had diffuse lymphadenopathy which subsided completely after therapy with p-di-(2-chloroethyl)-aminophenylalanine. The remission in both patients is still maintained three months later.

Carcinoma of the Lung.—Four patients with inoperable and rapidly progressive carcinoma of the lung were treated with p-di-(2-chloroethyl)-aminophenylalanine. One patient (case 16) with diffuse metastatic disease involving the pleura and treated with p-di-(2-chloroethyl)-aminophenylalanine has had a marked objective remission for 11 months. There has been improvement in well-being, weight gain, and increased aeration of the involved lung. Another patient (case 17) with inoperable bronchogenic carcinoma involving the lymph nodes has also shown a steady but general improvement and a gradual decrease in size of the tumor mass. Two other patients with disseminated bronchogenic carcinoma (cases 18 and 19), one after pneumonectomy, showed only minimal improvement after treatment with p-di-(2-chloroethyl)-aminophenylalanine.

Carcinoma of the Ovary.—Five patients with ovarian carcinoma were treated with p-di-(2-chloroethyl)-aminophenylalanine. Four of these patients had cystadenocarcinoma of the ovary and one had a granulosa cell carcinoma of the ovary. Of the four patients with cystadenocarcinoma (cases 20, 21, 22, and 23) three showed only slight objective improvement after p-di-(2-chloroethyl)-aminophenylalanine therapy. No effect was noted in the fourth patient (case 23). In the patient with granulosa cell carcinoma (case 24), a marked remission was obtained after administration of p-di-(2-chloroethyl)-aminophenylalanine. She was maintained in remission for one and one-half years and subsequently died as a result of intestinal obstruction. Autopsy findings revealed complete disappearance of all tumor masses noted during her laparotomy a year and a half before. Intestinal obstruction was caused by a fibrous tissue mass at the site of a previous tumor.

Carcinoma of the Uterus.—Two patients with malignant tumor of the uterus were treated. One patient with endometrial carcinoma (case 25), previously treated with triethylene thiophosphoramide, failed to respond to p-di-(2-chloroethyl)-aminophenylalanine therapy. One patient with fibrosarcoma of the uterus (case 26), whose tumor had been rapidly recurrent before therapy, remained free of tumor masses for eight months. Her general condition is well maintained and without obvious tumor recurrence at the time of writing.

Carcinoma of the Tongue.—Three patients with carcinoma of the tongue, previously treated by surgery and radiation, received p-di-(2-chloroethyl)-aminophenylalanine. One patient (case 27) developed a marked slough of the tumor mass. This remission was maintained for a four-month period, after which the tumor again started to grow rapidly. Two other patients (cases 28 and 29), also had an objective remission, manifest by a decrease in tumor size, with subsequent regrowth after a four-month interval.

Melanoma.—Four patients with melanoma were treated with p-di-(2-chloroethyl)-aminophenylalanine. The axillary tumor of one patient (case 30) measured 20 by 30 cm. Complete necrosis of the tumor mass occurred after she received p-di-(2-chloroethyl)-aminophenylalanine. This resulted in a constant large amount of serosanguineous discharge, which was not adequately replaced. The patient died about five weeks after initial treatment. At this time the entire tumor mass had become necrotic.

In another patient (case 31) one course of 150 mg. of p-di-(2-chloroethyl)-aminophenylalanine was given after removal of a large melanoma and its satellite from the back. There has been no evidence of any recurrence of any dissemination of the lesion during the nine-month follow-up period.

One other patient (case 32) with disseminated melanoma failed to show any response after administration of the drug. The remaining patient (case 55) was treated by perfusion and will be described subsequently.

Neurilemmoma.—P-di-(2-chloroethyl)-aminophenylalanine was administered to one patient (case 33) with widely disseminated neurilemmoma. Within the first month after treatment one mass, measuring about 25 by 40 cm., resolved to within one-third its original size. Other masses, however, although static for a while began to enlarge again, and her status subsequently deteriorated rapidly. Repeated courses of p-di-(2-chloroethyl)-aminophenylalanine therapy were without objective benefit.

Fibrosarcoma of the Back.—One patient (case 34), had a large fibrosarcoma of the back, measuring about 20 by 30 cm., which could not be removed completely. After operation he received 200 mg. of p-di-(2-chloroethyl)-aminophenylalanine. The residual tumor has disappeared and he remains free of disease eight months hence, at the time of writing.

Kaposi's Sarcoma.—The presenting features in the patient with Kaposi's sarcoma (case 35) were numerous subcutaneous nodules, enlargement of lymph nodes, and psoriasis. In addition to a course of therapy with 160 mg. of p-di-(2-chloroethyl)-aminophenylalanine, this patient received dexamethasone (Decadron) for the treatment of his dermatological disorder. An excellent remission has been obtained for nine months, and nearly all of the lymph nodes and subcutaneous masses that were previously palpable are no longer detectable. His general health is well maintained, at the time of writing.

Carcinoma of the Colon.—Eleven patients with carcinoma of the colon received p-di-(2-chloroethyl)-aminophenylalanine. One of these patients (case 59) was treated by segmental perfusion for a recurrent tumor mass in the perineal wound 15 months after an abdominoperineal excision of the rectum (Mile's operation). Another patient with recurrence two and one-half years after operation was treated by perfusion. Of the nine cases treated by oral administration, only two showed objective evidence of improvement. One patient (case 36), whose tumor was originally in the cecum and who had a local recurrence, developed a rapid increase in the size of her tumor mass after administration of p-di-(2-chloroethyl)-aminophenylalanine. During laparotomy a complete disappearance of numerous nodes, noted during the first operation, was revealed in the para-aortic chains, and, in addition, the tumor mass in the right lower quadrant was completely necrotic and contained liquefied hemorrhagic matter. A patient (case 37) whose status was terminal at the time therapy was instituted showed evidence of widespread abdominal dissemination after colonic resection, and there was fluid in both thoracic cavities. The pleural effusions were treated by the instillition of nitrogen mustard, and, in addition, she received p-di-(2-chloroethyl)-aminophenylalanine. During the ensuing three months there was no recurrence of fluid within the thoracic cavities, the ascites disappeared, and all tumor masses in the abdomen also disappeared. This was followed by a prompt reappearance of abdominal tumor masses and a steady downhill course.

Gastric Carcinoma.—One patient with carcinoma of the stomach (case 45), previously treated with triethylene thiophosphoramide, was treated with p-di-(2-chloroethyl)-aminophenylalanine. There was no objective evidence of any amelioration of the disease.

Various Malignant Diseases.—Other patients with such diseases as lymphoepithelioma (case 46), nephroblastoma (case 47), osteogenic sarcoma (case 48), and mucoid adenocarcinoma (case 49) were treated with p-di-(2-chloroethyl)-aminophenylalanine. There was no improvement afterward.

Also treated with p-di-(2-chloroethyl)-aminophenylalanine were patients with neurofibrosarcoma of the mesentery of the small intestine (case 50), prostatic carcinoma (case 51), malignant lymphoma (case 52), and laryngeal carcinoma (case 53).

Treatment with p-di-(2-chloroethyl)-aminophenylalanine was undertaken in case 50 after a palliative resection. At operation numerous involved nodes could not be removed because of their location in the root of the mesentery of the small intestine. Treatment was instituted with the hope of controlling this residual tumor. The patient received a total dose of 160 mg. initially. She has been maintained on therapy with 60 mg. of p-di-(2-chloroethyl)-aminophenylalanine every three months, bringing the total to 320 mg. at the time of writing. There has been no evidence of any abdominal tumor mass and this patient continues to remain in good health, 11 months later.

The patient with prostatic carcinoma (case 51) showed no response to 200 mg. of p-di-(2-chloroethyl)-aminophenylalanine. This patient had been previously treated by orchiectomy and administration of estrogen. The patient (case 52) with widely disseminated malignant lymphoma also failed to respond.

The patient with laryngeal carcinoma (case 53) showed evidence of some focal necrosis and decrease in size of the tumor mass. This patient died after a sudden hemorrhage of one of the great vessels of the neck, having received a total dose of 240 mg. of p-di-(2-chloroethyl)-aminophenylalanine.

Patients Treated by Segmental Perfusion with P-di-(2-chloroethyl)-aminophenylalanine

Seven patients were treated by segmental perfusion with p-di-(2-chloroethyl)-aminophenylalanine. In only five of these patients was the disease localized within the segment. The other two patients, one with bladder carcinoma and one with rectal carcinoma, showed evidence of hepatic involvement.

Carcinoma of the Female Urethra.—A female patient (case 54) with carcinoma of the urethra with extension to the inguinal lymph nodes was treated with p-di-(2-chloroethyl)-aminophenylalanine administered orally. During the ensuing 30 days after conclusion of therapy the ulcer in the right lower quadrant healed completely and the primary tumor decreased to about one-tenth of its original size. After six months, slow regrowth of a nodule in the right lower quadrant was observed and this patient subsequently underwent perfusion of the pelvic viscera with 150 mg. of p-di-(2-chloroethyl)-aminophenylalanine. Some changes were noted about the tumor within the first week, although the acute necrosis that had been noted in some instances of bladder tumor treated in this fashion had not been observed. Marked regression has since occurred and the lesion has now healed almost completely. There has also been a marked improvement in the patient's general condition.

Melanoma.—In another patient (case 55), after six operations for local recurrence of a lymphangiosarcoma of the left upper extremity, perfusion with p-di-(2-chloroethyl)-aminophenylalanine was undertaken. Although the histological study failed to reveal any residual tumor, the history indicated a rapid recurrence which prompted treatment by perfusion. No evidence of any recurrence has been noted during the six months after perfusion.

Carcinoma of the Bladder.—Therapy with p-di-(2-chloroethyl)-aminophenylalanine was undertaken in three patients with carcinoma of the bladder. The tumor areas were treated by perfusion of the pelvic viscera. About 150 mg. of intravenously given p-di-(2-chloroethyl)-aminophenylalanine was added to the extra corporeal circuit and circulation was maintained for about 15 minutes.

In case 56 the tumor mass was extremely large and involved the entire left lower quadrant, producing lymphedema of the left lower extremity. There was also hepatic involvement. A decrease in size of the tumor mass was noted during the first week after operation. There was also relief of pain after the perfusion. At the beginning of the second week this patient developed marrow depression and died. Autopsy findings revealed focal necrosis in the pelvic tumor mass and also in the hepatic nodules.

Another patient (case 57), whose situation was identical, experienced complete liquefaction of the tumor which drained subsequently through a sinus in the lower quadrant. The patient's postoperative course was complicated by wound dehiscence, but its surgical repair was without incident. However, both preoperatively and postoperatively, this patient had an unexplained high temperature. On his 13th postoperative day, after what appeared to be an unremarkable course (and by this time all drainage had ceased from the sinus), hyperpyrexia and evidence of marrow depression developed. This patient died.

The patient (case 58) whose tumor was confined to the bladder underwent perfusion (after performance of a biopsy) without incident. There were no signs of a recurrent malignancy during the postoperative course. A second biopsy performed seven days later showed necrosis at the side of the tumor. Despite all supportive measures this patient continued a slow downhill course and died. Autopsy revealed numerous renal abscesses. The site of the tumor was marked by an ulcer. There was only a small plaque of residual tumor.

Carcinoma of the Colon.—A patient (case 59) whose recurrence of carcinoma was in the perineum, was treated by perfusion of the lower abdominal segment. At laparotomy diffuse hepatic metastasis was revealed, in addition to the large pelvic mass. Perfusion was followed by complete disappearance of the perineal mass, healing of the biopsy site, and amelioration of pain. After two months there was some pain but no recurrence of the perineal mass. An unexplained observation is the complete loss of pubic hair and hair over the abdomen to the left of the midline in the segment which had been perfused. The possibility that the blood from the extracorporeal circuit was perfused largely through the left iliac artery is to be considered. This patient has since developed a metastasis to the right ischium. The perineal mass has not recurred to the time of writing.

One patient (case 60) had been operated on for carcinoma of the sigmoid two years prior to perfusion. This tumor had become recurrent, and at the time of perfusion the mass involved the retroperitoneal tissues behind the sigmoid and had extended anteriorly into the abdominal wall. The lower pelvis viscera were perfused, but in this patient 1 mg. per kilogram of body weight of p-di-(2-chloroethyl)-aminophenylalanine was added to the perfusant. Her recovery was uneventful. The mass in the abdominal wall, although still present, is now about one-fifth of its original size. An effect was noted in the mass within three days after perfusion. Her general condition remains good eight weeks after perfusion.

Comment

The result of this study indicates that some amelioration can be obtained by administration of p-di-(2-chloroethyl)-aminophenylalanine in certain types of malignant tumors in human beings. In the types in which effects have been noted, there have been varying degrees of response, including some instances in which no detectable effects have been observed, and other instances in which complete regression has taken place for a prolonged period. The reason for this, of course, is not known, but it would appear that some participation of host factors might also be necessary in order to obtain regression. The stage of the disease when therapy is instituted might also be an important factor. The most marked effects have been noted in patients with sarcoma, particularly in those with Hodgkin's disease, fibrosarcoma, Kaposi's sarcoma, and neurofibrosarcoma. A number of patients with carcinoma of the breast are apparently favorably affected by the drug. A marked effect, manifested as extensive necrosis, has been observed in a patient with melanosarcoma. Patients with carcinoma of the gastrointestinal tract are only slightly affected.

When p-di-(2-chloroethyl)-aminophenylalanine was introduced into an isolated segment by the previously described perfusion technique, two patients with gastrointestinal carcinoma had a decrease in size of the masses. The possible explanation of this may lie in the fact that the local concentration of the drug is higher when given by this route than by any other. Perhaps, if such high concentrations could be attained by oral administration, the effects could be reduplicated. Unfortunately, the only limiting factor is, of course, the effect on the marrow with such high concentrations.

Of the patients treated by perfusion, all, but the one in case 55 were perfused with 2 mg. per kilogram of body weight of p-di-(2-chloroethyl)-aminophenylalanine. Two of these patients showed profound evidence of marrow depression. In these patients the tumors were large and complete necrosis occurred after perfusion. It is possible that the products of tissue destruction contributed to the marrow depression, since other patients perfused with the same amount of the drug did not manifest the same effects.

Summary

Sixty patients with various malignant tumors were treated with p-di-(2-chloroethyl)-aminophenylalanine (Sarcolysin, Sarcolysine [nitrogen mustard]). With the usual orally administered dose, namely, 2 mg. per kilogram of body weight, profound effects on the marrow were rarely observed.

Sarcomas of varying types, especially Hodgkin's disease, appear to be the most susceptible tumors. Next in order of susceptibility are the melanomas and carcinoma of the breast. Occasional cases of

carcinoma of the lung, carcinoma of the tongue, carcinoma of the ovary, and carcinoma of the colon are susceptible, although for much shorter periods than the aforementioned tumors.

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Drs. S. Dana Weeder, Harry E. Knox, John H. Wolf, and Newton Masson assisted in this work.

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MANAGEMENT OF THE CHILD WITH THYROIDAL CARCINOMA

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According to the medical histories of 59 children having thyroid cancer, 58 had palpable masses in the neck which were not associated with preceding infections or systemic reactions. The neoplasm occurred most frequently in girls (40) and characteristically grew slowly. Often, early in the course of the disease, metastatic growths were found in the cervical lymph nodes. Two patients had tumors located in thyroid lobes directly under skin areas previously treated with roentgen rays, one for a hemangioma and another a keloid. Treatment of choice for such tumors in children, as in adults, is surgical excision when the lesion is considered operable. Radioiodine is of benefit when administered to selected patients with inoperable lesions. Those which do not accumulate iodine should be treated with roentgen rays or radium.

Carcinoma of the thyroid gland among children has been diagnosed with increased frequency during recent years.[1] At the same time, new techniques for the study and treatment of thyroidal disease have been described. The pediatrician who once thought of thyroidal carcinoma as a medical curiosity must now consider it in the differential diagnosis in any child seen with a nodular goiter or persistent cervical adenopathy.

Material and Background Data

It is the purpose of this presentation to relate experience gained in the management of children less than 15 years of age with carcinoma of the thyroid, who have been seen at the Mayo Clinic. In an earlier publication,[2] we reported observations on 41 children with thyroidal carcinoma who were seen before Jan. 1, 1955. Studies on these patients have been extended, and 18 new cases have been added. Two of this latter group were found in a review of pathological specimens removed from the thyroids of children and, therefore, should have been included in our earlier report. The remaining new patients were seen in the period Jan. 1, 1955, through May 31, 1959. The entire group of 59 patients included 40 girls and 19 boys. Figure 1 represents the distribution of patients according to year of diagnosis. The diagnosis of carcinoma was confirmed in every patient by careful examination of adequate pathological specimens.

Carcinoma of the thyroid may occur at any age. Nine of our patients manifested evidence of the disease before they were 5 years of age, although only one patient in this group was treated before this age. The distribution of patients according to age at time of onset of symptoms or signs is presented in figure 2. The average duration of symptoms or signs before the diagnosis was established was about two years, the range being from one

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day to 13 years. The distribution of patients according to age at time of diagnosis is presented in figure 3.

The report of Duffy and Fitzgerald [3] in 1950 has prompted much discussion of the possible relation between irradiation and carcinoma of the thyroid gland.[4] Among the 59 patients of this study, 30 are known to have had irradiation directed to the head, neck, or chest three or more years before the diagnosis of carcinoma of the thyroid was established. In 11 patients there is no history of irradiation, while information about the remaining 18 patients is not available (table 1). Three patients are of particular interest: One was born with a large solitary mass in the thyroid which, on removal at the age of 6 months, was proved to be a thyroid carcinoma; there was no history of the mother having been given irradiation. On the other hand, in two patients carcinoma of the thyroid developed in the lobes directly under areas treated with roentgen rays—in one instance for a small hemangioma, and in the other for keloid secondary to a burn.

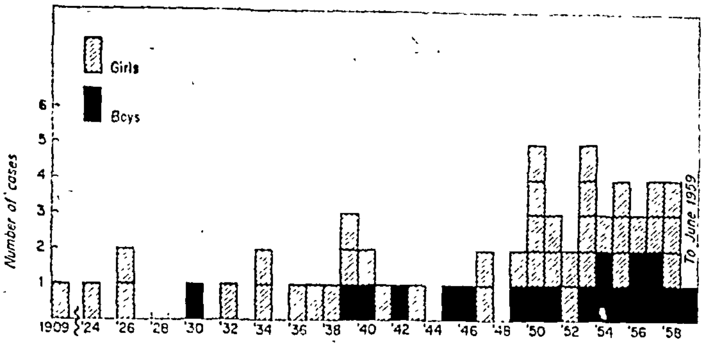

Fig. 1.—Distribution of patients according to year of diagnosis of thyroid carcinoma (total 59 cases).

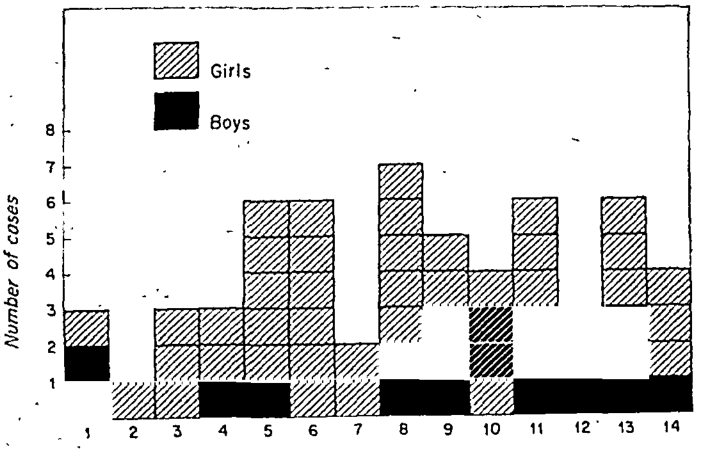

Fig. 2.—Distribution of patients according to age at time of onset of symptoms or signs.

In general, carcinomas of the thyroid can be divided into two groups, namely those of a low grade of malignancy, most of which are papillary, and those of a high grade of malignancy, which are the anaplastic carcinomas. The behavior pattern of each group of tumors is decidedly different from that of the other. Anaplastic tumors of the thyroid fortunately are extremely rare among children. When such lesions occur, they are rapidly invasive, do not respond to treatment, and cause death in a short period. Papillary carcinoma of the thyroid almost always grows slowly, although metastatic lesions appear early and may be extensive at the time the disease is recognized. Most such tumors respond to one or more types of treatment, and either cure or many years of palliation can be anticipated.

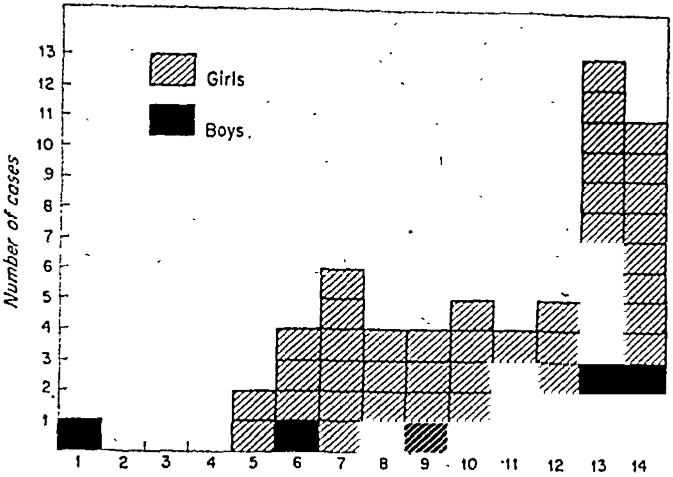

Fig. 3.—Distribution of patients according to age at time of diagnosis of thyroid carcinoma.

The diagnosis of thyroidal carcinoma can be established only by histological examination, but the disease presents a clinical picture that is so characteristic that it strongly suggests its presence. According to the case histories, 58 of the 59 patients had palpable masses in the neck that had not been associated with preceding infections or systemic reactions. Two patients complained also of respiratory obstruction, and another noted hoarseness. Only one patient was suspected of having hyperthyroidism. A small papillary carcinoma was

TABLE 1.—*History of Previous Irradiation Among Fifty-nine Children with Carcinoma of Thyroid*

	No. of Cases
No information available	18
No history of irradiation	11
Previous irradiation	30
Site of (and reason for) irradiation	
Chest (chronic cough)	6
Chest and nasopharynx (recurring upper respiratory infections)	1
Nasopharynx (recurring upper respiratory infections or obstructing adenoids)	7
Thymus	10
Neck	5
Chronic cervical adenopathy	3
Hemangioma of neck	1
Keloid after burn	1
Scalp (ringworm)	1

an incidental finding at the time of thyroidectomy for exophthalmic goiter in one patient. A total of 42 patients had palpable cervical lymph nodes as the result of the thyroidal carcinoma at the time of admission to the clinic; in 31 patients, the enlarged nodes were confined to one side of the neck, whereas they were palpable bilaterally in 11.

Twenty-three of the 59 patients had metastatic involvement of the lymph nodes on both sides of the neck at some time during the course of the disease. Eleven patients had palpable lesions of the thyroid alone, but 2 of these were found to have metastatic enlargement of the lymph nodes at the time of the operation, so that only 9 of the 11 were not proved to have metastasis. These 9 patients and the one in whom a small papillary carcinoma was found incidentally at thyroidectomy for exophthalmic goiter thus make a total of only 10 patients who were not proved to have metastasis to the cervical lymph nodes. The number of involved lymph nodes varied, but in most patients not more than three or four were palpable on the original examination. Lymph nodes affected by thyroidal carcinoma have a characteristic feel. They are firm, usually movable, nontender and discrete, and in most cases are members of the tracheoesophageal or jugular chain of nodes. The diameter of most of the nodes varied between 1 and 2 cm. In our experience, fixation or matting of the cervical lymph nodes by thyroidal carcinoma is seen only late in the course of the disease.

The thyroid should be carefully palpated in every child who has enlarged, nontender cervical lymph nodes. If enlargement of these nodes is the result of metastasis from thyroidal carcinoma, the thyroid will almost always be found abnormal on palpation. In most instances a firm, nontender nodule has been palpated, but in an occasional patient the gland has been described as diffusely enlarged or firmer than normal. In the present series, 53 patients were considered to have abnormality of the thyroid on palpation at the time of the original examination, and only 6 patients had small primary lesions of the thyroid that were not palpable before operation. Fifteen patients were considered on clinical examination to have abnormalities involving both lobes of the thyroid. We should like to emphasize that the presence of enlarged, firm, discrete, nontender lymph nodes in the cervical region, when associated with palpable abnormality of the thyroid, is strong evidence of thyroidal carcinoma.

Laboratory studies have been of little help in establishing the diagnosis of thyroidal carcinoma, although they sometimes aid in excluding other conditions.

TABLE 2.—*Thyroidal Carcinoma in Children: Classification of Cases*

	No. of Patients in Group*				
	A	B	C	D	E
Total patients	10	28	3	12	6
Male	4	8	0	6	1
Female	6	20	3	6	5
Pathological diagnosis					
Papillary carcinoma	5	28	3	11	6
Follicular carcinoma	4	...	...	...	...
Solid carcinoma	1	...	...	1	...
Nonsurgical treatment	7	13	3	8	6
X-ray	1	3	2	...	...
Radium	6	8	...	...	2
X-ray and radium	...	1	1	...	2
I^{131}	...	1	...	8	...
X-ray and I^{131}	...	...	...	...	1
Radium and I^{131}	...	...	...	...	1
Deaths	2 (1 surgical, 1 from carcinoma)	2 (1 proved, 1 presumed carcinoma)	2 (1 carcinoma, 1 sarcoma arising in neck)	1 (carcinoma ?)	2 (carcinoma)

* Group A: thyroidal carcinoma without metastasis, treated primarily by surgical excision; group B: thyroidal carcinoma with cervical metastasis, treated primarily by subtotal thyroidectomy and excision of nodes; group C: thyroidal carcinoma with cervical metastasis, treated by external irradiation alone; group D: extensive thyroidal carcinoma, treated primarily by total thyroidectomy; group E: inoperable thyroidal carcinoma.

Classification of Cases

In our earlier publication we arbitrarily divided the children seen at the Mayo Clinic because of carcinoma of the thyroid into five groups based on the type of treatment given at the time of the patient's original visit to the clinic. The relatively small number of patients, the difference in the degree of involvement by carcinoma, and the great variability in the types of treatment used make it apparent that no truly satisfactory grouping of patients is possible. It seems worthwhile, however, to continue the use of this grouping with slight modification (table 2).

Ten patients with carcinoma of the thyroid without metastasis make up group A. They were treated by surgical excision of the carcinoma. Seven of these patients were given external irradiation (six patients with radium, one with x-ray) during the postoperative period. One of the patients died of thyroidal carcinoma with pulmonary metastasis and another of respiratory obstruction 40 hours after excision of the tumor.

The 28 patients included in group B were, for the most part, seen initially by a physician because of enlarged cervical lymph nodes. In 17 patients the diagnosis was established by biopsy of these nodes before the patients arrived at the clinic or at the time of subtotal thyroidectomy. Each was treated by subtotal thyroidectomy and excision of involved cervical lymph nodes. Although the extent of the thyroidectomy varied considerably, in most instances total lobectomy and modified dissection of the neck were carried out on the affected side while the uninvolved lobe was subtotally removed. Twelve patients, all seen before 1951, were given external irradiation, and one was treated with radioiodine (I^{131}). Twelve patients have had one or more additional operations for removal of recurrent carcinoma in the thyroid or in cervical or substernal lymph nodes. Two deaths occurred in group B.

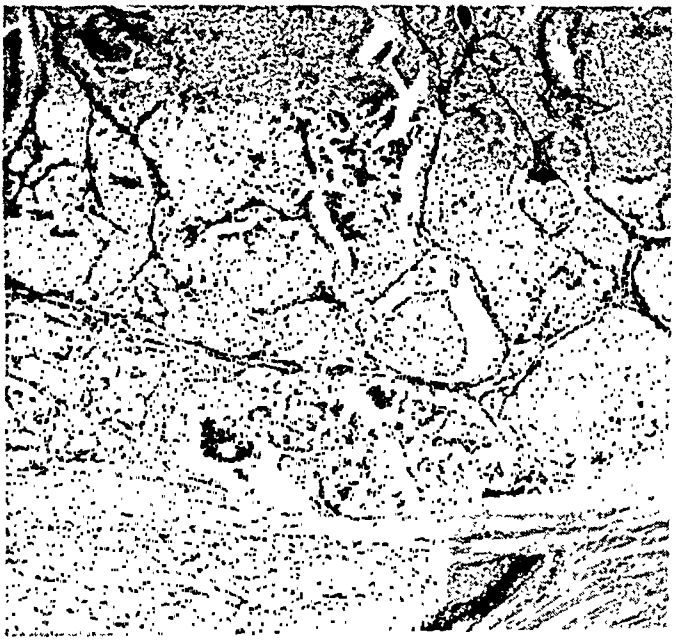

Fig. 4.—Histological section through typical papillary carcinoma showing mixture of papillary, follicular, and solid components. Hematoxylin and eosin stain (× 50).

The three patients of group C were treated with roentgen rays and radium alone, at least early in the course of the disease. The records indicate that they had no more extensive carcinoma than did the patients of group B, but they were electively treated with external irradiation. One of the patients, first seen in 1924 with papillary carcinoma involving the right lobe of the thyroid and metastatic spread to the cervical lymph nodes, underwent x-ray therapy for 18 years. Metastatic spread to the thorax was first noted in 1943, and the patient died in 1945. The second patient, first seen in 1934 because of papillary carcinoma of the left lobe of the thyroid with metastatic spread to the cervical lymph nodes, received x-ray and radium therapy for many years. At the time of her last examination in 1958, there was no definite evidence of residual thyroidal carcinoma, but she had disturbing actinodermatitis of the neck and upper part of the thorax. The third patient, seen in 1940 because of carcinoma of both lobes of the thyroid with metastasis to the cervical lymph nodes on the left, received x-ray therapy both at the clinic and in her home community. In 1957 she developed a rapidly growing cervical mass which was histologically proved to be a highly malignant sarcoma. She died in May, 1957.

Group D is made up of 12 patients, seen since 1952, with extensive papillary carcinoma of the thyroid. Each underwent total thyroidectomy with removal of cervical lymph nodes. In 11 of the 12 patients it was necessary to remove involved cervical nodes from both sides of the neck, and in the one patient with unilateral involvement of the neck both lobes of the thyroid had been replaced by carcinoma. Eight patients of this group, including three with pulmonary metastasis, have been treated with I^{131}. The progress of one patient who underwent total thyroidectomy in 1952 has not been followed at the clinic since 1954, and we have just learned of her death. The remaining three patients are still under observation and manifest no evidence of residual carcinoma. Persistent hypoparathyroidism, a most disturbing complication of total surgical thyroidectomy, ensued in 11 of the 12 patients of this group.

Group E comprised six patients who were seen at the clinic before 1948 and were considered to have inoperable carcinoma of the thyroid at the time of their first visit. All were treated with I^{131}, radium, or roentgen rays, singly or in combinations. Extensive infiltration of the recurrent laryngeal nerves, trachea, or esophagus and metastasis to the lungs were the criteria by which these tumors were judged inoperable. Two deaths occurred in group E. It is remarkable that four of these patients were living and well when last contacted 11 to 27 years after the diagnosis of thyroidal carcinoma had been established.

Pathological Aspects

Thyroidal carcinomas may be classified into four main histological types. The most common is papillary carcinoma, a slowly growing, typically unencapsulated tumor which metastasizes mainly to regional lymph nodes. The second type, also slowly growing, is termed "follicular carcinoma." This is usually an encapsulated lesion that tends to infiltrate vessels or surrounding thyroid and metastasizes via the blood stream to the lungs or bones. The third type, which grows rather slowly, is termed "solid carcinoma" on the basis of its microscopic architecture, the cells occurring in nests or sheets without papillary projection or follicle formation. The stroma may present a peculiar hyaline or amyloid-like change. Tumors of this type may metastasize to nodes or distant sites. The fourth type, anaplastic carcinoma, grows rapidly and presents a number of microscopic patterns, among which the spindle and giant cell varieties are common. To this list must be added the occasional primary thyroidal malignant lymphoma.

Carcinoma of the thyroid in children is predominantly of the papillary type. Of our 59 cases, 53 were of the papillary type, 4 of the encapsulated follicular type, and 2 of the solid-carcinoma type. No examples of anaplastic carcinoma, Hürthle cell carcinoma, or primary lymphosarcoma were encountered.

Microscopic examination in papillary carcinoma reveals a spectrum of architecture that varies from that of purely papillary to that of almost purely follicular structure, but in most cases the tumor is composed of a mixture of neoplastic follicles and papillary projections (fig. 4). In addition, a more cellular solid component is frequently encountered. Psammoma bodies are seen in many cases. In those cases in which neoplastic follicles with good production of colloid make up the bulk of the tumor, satisfactory concentration of I^{131} may be demonstrated. In tumors that are predominantly papillary there is little or no concentration of the isotope. In general, the gross extent of the lesion when first seen, rather than the microscopic architecture, appears to be the more important consideration in management of the individual patient and in prognosis.

Grossly, papillary carcinoma is, with a few exceptions, an unencapsulated and invasive lesion that infiltrates thyroid parenchyma and shows varying degrees of sclerosis within the tumor tissue. The size of the primary lesion varies greatly. At the one extreme are those primary carcinomas, usually less than 1 cm. in diameter, that are associated with bulky nodal metastasis (occult papillary carcinoma of the thyroid) (fig. 5*a*). In this series there were six lesions of this type, the thyroid gland being, as a rule, impalpable on clinical examination. At the other extreme are those cases in which the bulk of the thyroid is replaced by papillary carcinoma, sometimes with extension beyond the capsule into adjacent structures (fig. 5*b*). The presence or absence of extension of the primary lesion beyond the thyroid capsule is of importance in that a recurrence in the midline of the neck with encroachment on the larynx or trachea is, in tumors of the papillary variety, a potential threat to life. Most primary papillary carcinomas in this series were confined to the thyroid itself.

Metastasis to cervical nodes was noted in 47 of 53 cases of papillary carcinoma, an incidence that is considerably higher than that seen in similar lesions in adults. As a rule, the metastatically involved nodes are large and discrete, and there is no infiltration of tumor beyond the capsule. Cystic and calcareous degeneration may occur. The total number of nodes that were proved to be involved in a single case varied from 1 to 34, involvement of multiple nodes being the usual finding. Pulmonary metastasis was diagnosed on the basis of roentgenographic findings in eight patients. In an additional patient the diagnosis of pulmonary metastasis was based on marked concentration of I^{131} in both pulmonary fields, although the results of roentgenographic examination of the thorax were considered normal. No distant metastasis, other than pulmonary, was proved in any case although suspected in one.

One patient having papillary carcinoma, with roentgenographic evidence of pulmonary metastasis when first seen, is worthy of special comment. After removal of a cervical node for diagnosis, the patient was given extensive x-ray therapy to the cervical region. Fourteen years later a second cervical node was removed and more x-ray therapy was given. Eighteen years after the original diagnosis a massive tumor developed in the anterior part of the neck, and the patient died of widespread disease within a few months. Histologically, the lesion was an anaplastic spindle cell neoplasm believed to be a radiation-induced sarcoma.

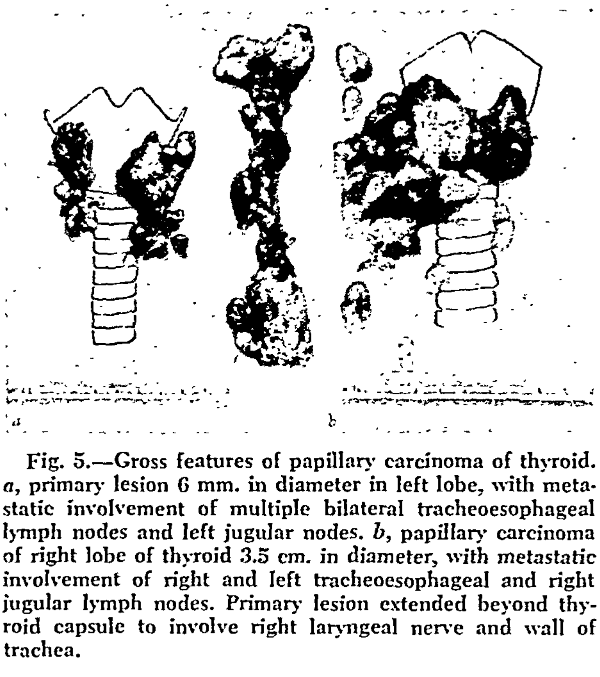

Fig. 5.—Gross features of papillary carcinoma of thyroid. *a*, primary lesion 6 mm. in diameter in left lobe, with metastatic involvement of multiple bilateral tracheoesophageal lymph nodes and left jugular nodes. *b*, papillary carcinoma of right lobe of thyroid 3.5 cm. in diameter, with metastatic involvement of right and left tracheoesophageal and right jugular lymph nodes. Primary lesion extended beyond thyroid capsule to involve right laryngeal nerve and wall of trachea.

Follicular carcinoma was found in four cases. Lesions of this type were grossly encapsulated and showed rather minimal evidence of infiltration. Definite vascular invasion, however, was demonstrated in one case. No involvement of lymph nodes was found in this group at the time of operation. One patient, an infant, died postoperatively. The progress of the other three patients has been followed for 9 to 32 years without evidence of nodal or distant metastasis.

Of the two patients with solid carcinoma, one had no evidence of metastasis at the time of operation and died 20 years later, with evidence of cervical and distant metastasis. The other had bilateral metastasis to the cervical nodes at the time of operation and died eight years later of shock after cesarean section; postmortem examination disclosed metastasis to the lungs and liver and bilateral pheochromocytoma.

Surgical Treatment

The treatment of thyroidal carcinoma in children is similar to that in adults. The treatment of choice is surgical if, on clinical examination, the lesion is thought to be operable. Even if there is some question as to operability, all lesions should at least be explored to obtain tissue for histological study and frequently for removal of the bulk of the accessible portions of the thyroid and the carcinoma so that the remaining portions may be more easily treated by other means. Prior to operation for a nodular goiter, whether or not the lesion is suspected of being carcinoma, the lateral cervical regions should be examined carefully for any evidence of metastasis, so that the surgical procedure can be better planned.

The thyroid should be explored through the usual collar incision. After the strap muscles have been spread and retracted laterally, the thyroid is exposed and any tumor is carefully examined. If there is gross evidence of carcinoma, the surgeon is justified in proceeding with total lobectomy on the side of the lesion, taking precautions to preserve the recurrent laryngeal nerve and, if feasible, parathyroid tissue.

The tracheoesophageal nodes are the ones most frequently involved in the presence of papillary carcinoma of the thyroid; hence, they should always be explored and removed if there is any question of involvement. The midjugular and the lower deep jugular groups of nodes are the next most commonly involved. Metastatic lesions in the upper deep jugular group of nodes are found less frequently. If extensive nodal involvement is present in the lateral part of the neck, radical cervical dissection is considered the best procedure. In most cases, however, in which nodal metastasis is present, a modified dissection of the neck will suffice. This procedure varies in extent as the findings dictate; all groups of involved nodes, node-bearing fascia, and fat should be removed. The internal jugular vein, as well as adjacent muscles in the area of involvement, may likewise have to be sacrificed.

Metastatic papillary carcinoma from the thyroid tends to remain encapsulated for long periods. On occasion it has been necessary to excise another node or group of nodes when metastasis has become apparent at some time after the initial spread. A third operation is rarely indicated. If nodes are not clinically palpable in the neck and none is discovered at the time of operation, the contents of the lateral part of the neck are not disturbed. Of 136 patients with papillary carcinoma of the thyroid representing all age groups and receiving definitive treatment in accordance with these principles, none subsequently had an inoperable recurrence because of inadequate treatment of cervical metastatic lesions.[5] Because of this experience, we believe that radical dissection of the neck is not indicated in the great majority of patients with papillary carcinoma of the thyroid. In the series of children with this disease, radical dissection of the neck has been considered necessary in only one instance. If the carcinoma is well localized, only partial lobectomy is performed on the contralateral side in addition to lobectomy on the affected side. The partial lobectomy not only preserves thyroid tissue for normal metabolic function but also protects the corresponding parathyroid glands. If the carcinoma is situated in the isthmus of the thyroid, extensive subtotal thyroidectomy should be performed; a remnant equal to 1 to 2 Gm. of tissue on either side should be preserved. If the primary lesion is multicentric (as in 10 to 20% of patients in all age groups) and involves both lobes, total thyroidectomy should be performed.

When distant or local metastasis or extension of the primary tumor makes the lesion inoperable, the surgeon is still justified in considering and performing, if possible, total thyroidectomy. This facilitates possible treatment of the remaining carcinoma by I^{131}. In the absence of all thyroid tissue, some carcinomas will function sufficiently to accumulate therapeutic amounts of I^{131}.

Total surgical thyroidectomy is frequently followed by parathyroid insufficiency, a complication that is serious enough to contraindicate this procedure unless the seriousness of the carcinoma makes it specifically indicated. This is usually a complication of operation when wide-field total thyroidectomy is necessary.

On rare occasions, a recurrent laryngeal nerve is injured accidentally. It may be sacrificed intentionally, however, if it is necessary to circumvent the lesion.

There has been one death due to operation among the 50 patients treated primarily by surgical means. This patient, an infant aged 6 months, died in 1940 after removal of a large carcinoma from the left lobe of the thyroid.

Use of Radioiodine

Radioiodine has proved useful in the treatment of certain patients with inoperable carcinoma of the thyroid. The successful use of this agent depends on the ability of the carcinoma to selectively accumulate iodine in sufficient concentration to be lethal to the malignant cells. At the same time, the amount of I^{131} given must be small enough to avoid severe irradiation injury to the hematopoietic system.

Carcinomas of follicular structure are more likely to accumulate iodine than are carcinomas of papillary structure, although an occasional tumor of predominantly papillary structure may accumulate significant amounts of I^{131}. Normal thyroid tissue usually accumulates iodine more readily than does carcinomatous thyroid tissue; therefore, it is necessary to remove the normal thyroid tissue which is competing with the carcinomatous tissue for the administrated I^{131}. Normal thyroid tissue may be removed either by the administration of I^{131} or by surgical excision. We have come to prefer the latter method of treatment, since it avoids the additional hazard of administering the large amount of I^{131} necessary to accomplish destruction of both normal thyroid gland and carcinoma. As a rule, surgical removal is a more certain method of ablating the normal thyroid, but its use adds the possible complication of hypoparathyroidism.

In the absence of normal thyroid tissue the iodine-accumulating ability of thyroidal carcinoma is best estimated by the administration of a tracer dose of I^{131}. The amount accumulated in the neck or in metastatic growths may be measured. At the same time, the total I^{131} retained is estimated by measuring the percentage of the total dose excreted in the urine during the 24 or 48 hours after administration of the test dose. The test dose should be large enough to assure definite localization in small metastatic deposits. In our experience, a total dose of 100 to 300 μc has proved satisfactory.

Radioiodine was used as a therapeutic agent in 11 children in this series. Two of the patients were treated with it in an effort to destroy normal thyroid tissue and residual carcinoma. They were given I^{131} in three divided doses over a period of about nine months, the amounts given totaling 119.5 and 175 mc. respectively (the first dose in each case having been given to destroy the normal thyroid tissue). In the second of these patients depression of the bone marrow developed; slow but finally complete recovery followed. The third patient was given 50 mc. of I^{131} after subtotal resection of the thyroid when studies of I^{131} uptake indicated that the carcinoma had a marked avidity for radioiodine. The remaining eight patients to whom I^{131} was given as a therapeutic agent were noted to have evidence of residual carcinoma, as indicated by I^{131}-tracer studies made after total surgical thyroidectomy. In three of the patients there was evidence of metastatic spread to the lungs; this spread was proved in two patients by roentgenograms of the thorax and by increased uptake of I^{131} by the lungs and in the third by increased radioactivity over the lungs without roentgenographic evidence of metastasis. Two of the three patients with metastasis to the lungs were given 648 and 335 mc. of I^{131}, respectively, in divided doses over a period of months; in each instance there has been evidence of resolution of the metastatic lesions in the lungs. The third patient with metastasis to the lungs is presently being treated with I^{131}. The remaining five patients treated with I^{131} after total surgical thyroidectomy had evidence of residual thyroidal carcinoma in the neck or upper part of the mediastinum as indicated by studies of I^{131} uptake. They have been treated with total doses of I^{131} that varied between 100 and 195 mc., and in each instance subsequent studies of uptake have indicated resolution of the metastatic deposits.

It is our policy to determine the uptake of I^{131} in all patients subjected to surgical total thyroidectomy within a few days after the operation. If there is evidence of iodine accumulation, a therapeutic dose is administered. In an occasional patient, thyrotropin is administered in doses of 10 international units daily for three to five days before the therapeutic dose is given, although we are not convinced that it significantly increases the uptake of iodine in metastatic deposits. After the I^{131} accumulation from the therapeutic dose has been estimated, the patient is given desiccated thyroid in physiological amounts and is advised to return for reexamination after three to six months, depending on the extent of the carcinoma and the size of the therapeutic dose of I^{131} that has been administered. One month before the anticipated date of return, the use of desiccated thyroid is discontinued to allow the development of myxedema. On the patient's return, a tracer dose of I^{131} is again administered, and the need for further therapeutic doses is determined.

Sodium liothyronine (L-triiodothyronine) may be given as indicated to hasten the recovery from myxedema, or it may be used instead of desiccated thyroid in the control of myxedema. If sodium liothyronine is used to correct hypothyroidism, it is not necessary to discontinue its use until two weeks before the anticipated date of the patient's return for the I^{131} study.

The dose of I^{131} used in therapy for carcinoma of the thyroid varies, depending on the accumulation of radioactivity in the tumor, the extent of the tumor, and the size of the patient. In most instances the therapeutic dose varies between 75 and 150 mc. The largest total amount of I^{131} administered to a patient with carcinoma of the thyroid in our series was 648 mc.

Other Therapy

Roentgen-ray and Radium Therapy.—Roentgen rays and radium are of proved value in the treatment of certain children with carcinoma of the thyroid.[6] Prior to 1950 it was our practice to treat all carcinomas of the thyroid with external irradiation after operation, even though the surgeon may have been confident that all the carcinoma had been removed. Since 1950 we have reserved the use of these agents for patients with inoperable carcinoma of the thyroid who cannot be treated with I^{131}.

Therapy with Thyroid Hormone.—It has been suggested that certain papillary carcinomas of the thyroid undergo regression after the administration of large doses of thyroid hormone.[7] We have not felt justified in delaying what we consider to be more definitive treatment for long enough periods to appraise the effect of thyroid hormone on carcinoma of the thyroid. We have, however, administered thyroid hormone in adequate amounts to all patients with thyroidal carcinoma.

TABLE 3.—*Survival Data* of Children with Thyroidal Carcinoma*

Survival Period, Yr.	Patients: Total	Patients: Traced	Lived Beyond Indicated Period: No.	Lived Beyond Indicated Period: % Traced
3	46	46	45	97.8
5	39	38	37	97.4
10	22	21	19	90.5
15	17	16	14	87.5
20	11	9	6	66.7
25	6	6	2	33.3
30	4	4	1	25.0

* Inquiry as of Jan. 1, 1959.

Results of Treatment

Nine deaths occurred among the 59 patients. One patient, an infant noted to have an enlarging mass of the left side of the neck at birth, was first seen at the Mayo Clinic in 1940 at the age of 6 months. The mass was confined to the left side of the neck and produced respiratory distress. The infant died of respiratory insufficiency 40 hours after surgical removal of a 25-Gm. tumor of the left lobe of the thyroid. The tumor was considered to be a benign adenoma, but reexamination of the tissue disclosed papillary carcinoma. The remaining eight deaths occurred within a period of a few months to 31 years after the diagnosis of carcinoma of the thyroid had been established. In seven patients, including the one previously referred to who had sarcoma, thyroidal carcinoma is known to have been the cause of death; in one instance it is presumed that carcinoma of the thyroid caused death. The data on survival are summarized in table 3.

Metastatic involvement of the lungs is known to have occurred in 11 patients, including 7 of those who died. Metastasis to the cervical lymph nodes occurred in 49 of the 59 patients. Metastasis to bone was not proved in any patient but was suspected in one. Hypothyroidism is known to have occurred in 25 patients, including the 14 patients subjected to total thyroidectomies (12 surgical and 2 I^{131}-induced). No effort has been made to establish the diagnosis of hypothyroidism among the patients seen in recent years, since we administered desiccated thyroid to all children with carcinoma of the thyroid as soon as the diagnosis was established. Permanent hypoparathyroidism occurred in 11 of the 12 children treated by total surgical thyroidectomy.

Summary and Conclusions

Carcinoma of the thyroid in children is a relatively rare condition which has been recognized with increased frequency during recent years. It occurs more frequently among girls than boys, the ratio being 2 to 1 in our series of 59 cases. The diagnosis is established by biopsy, but the disease should be suspected in any child with nodular goiter or persistent cervical adenopathy. Carcinoma of the thyroid in children almost always grows slowly, although metastasis occurs early and may be extensive at the time the disease is recognized. The method of treatment depends on the type and extent of the carcinoma. Whenever possible, all carcinomas should be surgically excised. When complete surgical excision is impossible, radioiodine (I^{131}) should be given, provided the tumor will accumulate iodine. Tumors that will not accumulate iodine should be treated with roentgen rays or radium.

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AN OUTBREAK OF SPOROTRICHOSIS IN FLORIDA

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Sporotrichosis infections occurred in eight workers at two separate pine tree nurseries in northern Florida. In one patient the infection was limited to the site of inoculation, and the others had the localized lymphatic type; all were cured by administration of iodides. This was the first incidence of the disease at either of the nurseries, one having been in operation for four years, the other for eight. Both have used the same procedures in planting, growing, harvesting, and shipping the young trees. The only change in routine that might be related to appearance of the disease was in the source of their supply of sphagnum moss, which is packed around the tree roots before they are shipped. Whether the moss, purchased from a different part of Wisconsin than before, contained the parasitic Sporotrichum schenckii has not yet been determined.

The clinical manifestations and mycology of sporotrichosis have been well described.[1] Infection in human beings most frequently is associated with injury by plant material or wood since the causal agent, Sporotrichum schenckii, is widely distributed as a saprophyte on various plants, shrubs, and elsewhere in nature. Indeed, the frequency of cases among farmers, gardeners, and horticulturalists has led Foerster to term sporotrichosis a true occupational disease.[2] The various plant materials that have been implicated in the disease include rose bushes, cactus, salt meadow hay, barberry, carnations, and wood splinters. Of particular interest is the report by Gastineau[3] of six cases associated with sphagnum moss.

The present report describes an outbreak of sporotrichosis among workers at two pine tree nurseries in northern Florida. The operation at both locations is identical and consists of harvesting and planting pine seeds, harvesting the young trees, and wrapping the roots of the young trees in wet sphagnum moss for packing and shipping. Although these nurseries have been in continuous operation for four and eight years, respectively, this was the first time the disease had been observed.

Since this represented the first appearance of this disease in many years, an attempt was made to find a change of routine which could be correlated with the appearance of the disease. The only change noted was that the sphagnum moss, which in past years had been obtained from the same dealer in Wisconsin (an endemic area), was now procured from a different dealer in another town in Wisconsin. Wisconsin public health officials are, at the time of this writing, investigating this possibility. In every instance the subject had contact with the sphagnum moss.

Bacteriological Studies

Direct smears of pus stained by both Gram and Gridley techniques failed to show any fungus. In all cases in which material could be obtained cultures were made. Pus from lesions was placed on freshly prepared slants of Mycosel agar (Baltimore Bacteriological Laboratories), which were incubated at room temperature. When growth appeared, after 2 to 14 days, subcultures were made to blood agar which was incubated at 37° C (98.6 F). In addition, the mycelial growth from the Mycosel agar was emulsified in 5% hog gastric mucin solution and injected intraperitoneally into mice. In each of the positive cultures obtained, conversion to the yeast phase occurred on blood agar subcultures, and typical gross and microscopic findings were obtained in the injected animals.

In addition to cultures of the lesions, samples of soil, pine needles, pine seeds, dust, and sphagnum moss were examined, both by culture on membrane filters and injection into animals.[4] The cultures became overgrown with other fungi, and repeated attempts to infect animals failed. Agglutinin studies were performed with use of the yeast phase antigen of Norden,[1b] and skin tests were done with use of the same antigen in a dilution of 1:1,000.

Report of Cases

Case 1.—A 26-year-old nurseryman's helper began work in December, 1958. His main job was handling and bundling pine trees with sphagnum moss. He frequently noted pricks and scratches from pine needles on his arms. During the last week of January, 1959, a small pimple appeared midway down on the extensor surface of his right arm. The lesion enlarged to the size of a quarter in three weeks and began draining purulent matter. About six weeks after the onset, a series of 8 or 10

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tender elevated erythematous nodules appeared along the lymphatic channel draining the granulating lesion. There was no history of chills or fever. The physical examination showed normal findings except for a 3-by-5 cm. granulating lesion on the extensor surface of the middle third of right arm with 12 elevated 1.5-by-1.5 cm. fluctuant nodules along the medial aspect of the right arm (fig. 1). The skin test showed positive results in 48 hours. Purulent material obtained by needle aspiration of a fluctuant nodule showed S. schenckii on culture. The lesions rapidly regressed and healed without suppuration over a period of six weeks, during which 4 Gm. of potassium iodide was used daily.

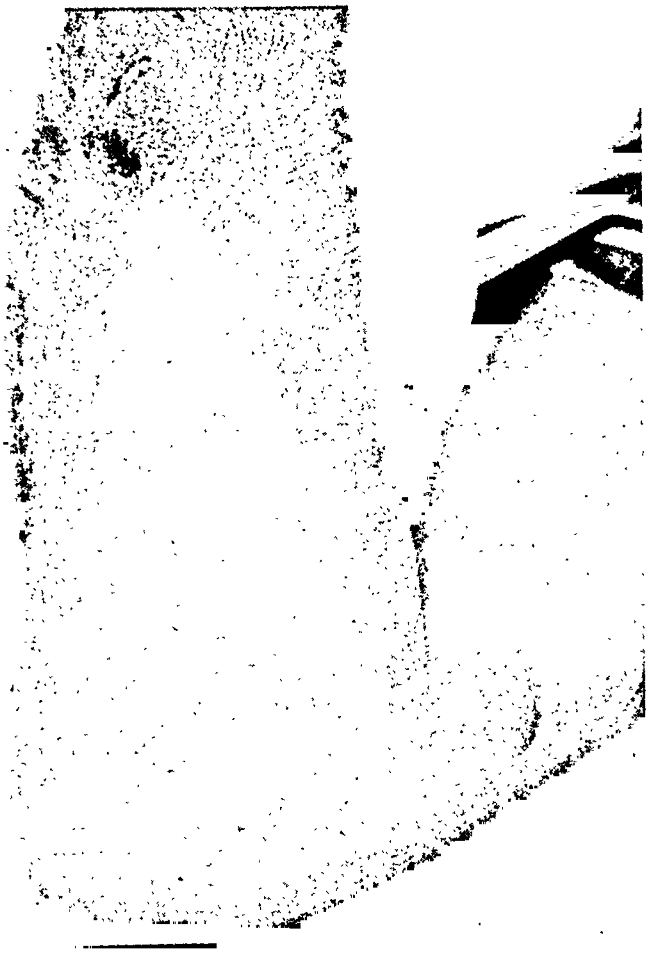

Fig. 1 (case 1).—Primary lesion with lymphangitis and nodules.

Case 2.—A 50-year-old nurseryman's helper had been working for several years handling moss, preparing the land, gathering trees, and participating in nearly all phases of the nursery activity. In October, 1958, while unloading sphagnum moss imported from Wisconsin, he pierced the lateral aspect of his left foot near the small toe with his pitchfork. An ulcerated area appeared between one and two weeks thereafter and became quite inflamed and indurated. He showed no lymphangitis or systemic symptoms. He sought no medical attention and continued to work. This lesion remained unchanged and continued to drain a thin white fluid over the next six months. The general physical examination showed negative results except for the necrotic lesion on the lateral aspect of the foot (fig. 2). The lesion measured 3 by 5 cm., was indurated, and had a thin crust. On manipulation it exuded a thin bloody exudate which on culture showed S. schenckii. A skin test revealed a 20 mm. induration in 48 hours. Agglutinins for sporotrichosis showed a final value of 1:160 for dilution of serum. The patient was given 15 drops of potassium iodide three times a day; this dosage was gradually increased to 40 drops during subsequent weeks, and the lesion healed during a period of three months.

Case 3.—A 30-year-old nurseryman's helper had been employed at the same occupation since 1955 and engaged in all of the activities of the nursery. On Jan. 6, 1959, he noted a small pimple on the extensor surface of the right arm. It became inflamed, and in two weeks he had increasing induration and a streak up his right arm. A red "kernel" appeared in the epitrochlear area, and numerous nodules appeared along the medial aspect of the lymphatic chain as well as on the lateral aspect of the arm. The primary lesion, measuring 3 by 4 cm., persisted on the extensor surface of the right arm. Each nodule suppurated spontaneously and drained white blood-tinged material. He noted on many occasions that while harvesting pine trees

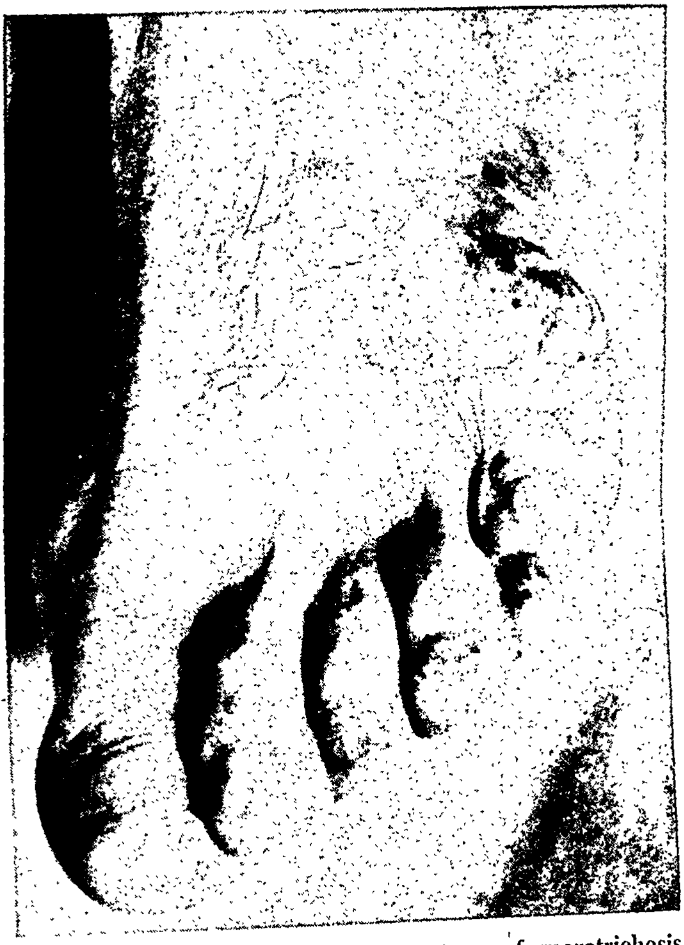

Fig. 2 (case 2).—Fixed cutaneous type of sporotrichosis occurring after pitchfork penetration.

with his hands the pine needles would prick him primarily in the extensor aspects of the arms. He experienced no significant systemic symptoms. The general physical examination revealed a large primary lesion on the extensor surface of the right arm 4 to 5 cm. above the ulnar aspect of the wrist. The lymphatic channels which drain this area were extensively involved and had ulcerations and indurations of 8 to 10 nodules (fig. 3). A culture of this lesion showed positive results for S. schenckii. A skin test showed positive results in 48 hours. Blood agglutinins showed a final value of 1:320 for dilution of serum. The patient was treated with 30 drops of strong iodine (Lugol's) solution three times a day and noted a gradual improvement in his lesions. He had also received x-ray therapy in this area.

Case 4.—A 40-year-old nurseryman's helper had been employed at this same occupation for several years. He helped in packing the trees with moss. On Jan. 10, 1959, he noticed a small pimple appearing on the extensor surface of the left arm. There was no history of trauma. He experienced no systemic symptoms. The area began to enlarge, and a red streak appeared on the left arm. On Jan. 22 he noted six to eight nodules along the epitrochlear lymphatic chain. They became tender, and he was initially treated with antibiotics and surgical drainage by his physician. Ultimately he was given 12 drops of potassium iodide two times a day. The lesions appeared to improve. Physical examination at this time revealed a large 3-by-5-cm. granulating ulceration of the left arm with a string of 8 to 10 nodules along the medial aspect of the left arm. On manipulation they drained a white blood-tinged fluid. The skin test showed positive results in 48 hours. Agglutinins showed a final value of 1:80 for dilution of serum. Culture of the lesion showed negative results for fungi. The patient showed gradual improvement on iodide therapy, and his lesions healed over a period of six months.

Case 5.—A 24-year-old nurseryman's helper had been employed at the nursery since December, 1958. On Feb. 15, 1959, while baling small pine trees with wire, he was struck by a piece of steel in the extensor surface of the thenar space on the left foot. This area never healed, and a small pustule appeared and ulcerated. One to two weeks later he developed lymphangitis of the left arm. He was subsequently treated with 10 drops of potassium iodide three times a day. The tenderness of the nodules gradually diminished, but they became indurated. Several spontaneously suppurated and drained thin white material. There were no systemic symptoms. The general physical examination showed negative findings except for the 2-by-3-cm. granulating ulceration of the thenar space on the left foot with a chain of 10 nodules along the ulnar aspects of the left arm extending to the middle of the arm. Several suppurated and drained white material. Culture of this material revealed S. schenckii. A skin test showed positive results in 48 hours. Agglutinins showed a final value of 1:160 for dilution of serum.

Case 6.—A 40-year-old handyman who occasionally handled the pine tree and moss first noted in January, 1959, the appearance of a small bump on his right arm which gradually enlarged to a 3-by-5-cm. ulceration. Two weeks later a red streak appeared on this arm, and then five or six nodules appeared. He noted slight fever and malaise. He received penicillin injections but showed no improvement. The lymphangitis and primary lesion spontaneously began to heal, and the entire inflammatory process lasted for a period of six weeks. He received no iodide therapy. A residual 2.5-by-3.0-cm. scar remained at the primary site. Skin test showed positive results; agglutinins showed a final value of 1:40 for dilution of serum. No growth was obtained on culture of the residual scar.

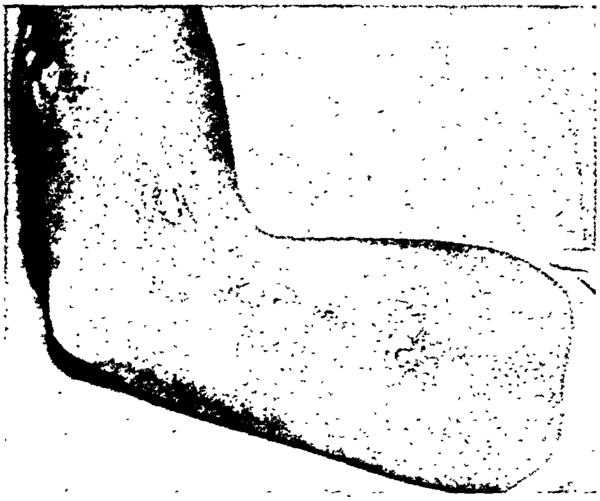

Fig. 3 (case 3).—Primary lesion and suppurated nodules which have become crusted and indurated after three and one-half weeks of iodide therapy.

Case 7.—A 23-year-old equipment operator at the nursery, who was involved in the same routines as the patient in the previous case, noted on Jan. 15, 1959, a small pimple on the middle finger of the right hand; it became indurated, red, and subsequently ulcerated. In two weeks a string of red and tender lymphatic nodules appeared on the extensor surface of his right arm. After the patient was treated with iodide there was considerable improvement, and resolution of the process took place over the next three months. The skin test showed positive results. Agglutinins showed a final value of 1:160 for dilution of serum. The culture showed negative results.

Case 8.—A 25-year-old equipment operator at the nursery worked on the processing of the pine trees. On Dec. 15, 1958, he noted on the flexor aspect of his left wrist a small bump which increased rapidly to the size of a quarter and exuded a thin white discharge. Treatment with antibiotics was ineffective. Two weeks later lymphangitis ensued, and later the nodules suppurated, with multiple draining indurated areas. He was subsequently treated with iodides and roentgenographic therapy and showed gradual improvement. The skin test showed positive results. Agglutinins showed a final value of 1:160 for dilution of serum. The culture showed positive results for S. schenckii.

Comment

The vast majority of cases, as in this outbreak, are of the localized lymphangitic type. Case 2 was the only exception and is an example of the fixed cutaneous form which occurs when the process is limited to the site of inoculation. We did not encounter other variations of this diease, which include disseminated sporotrichosis and involvement of the bone,[1a] eye,[5] viscera, and other organs.[6]

Frequently there is a history of minor trauma preceding the appearance of a small pimple or pustule. Although only two of our cases were clearly associated with trauma, the nature of the patients' work and the handling of the sharp pine needles probably provided an adequate mode of inoculation with S. schenckii. Each patient gave a history of the appearance of a painless pimple or pustule followed in one or two weeks by a series of subcutaneous nodules along the path of lymphatic drainage of the primary site. They became quite tender, and the lymphatic vessels felt cordlike. The process remained well localized to an involved area and rarely produced systemic symptoms. Spontaneous healing, though rarely observed, occurred in the patient in case 6 with a total duration of illness of six weeks. The clinical picture of a primary granulating or ulcerated lesion with lymphangitis and nodules in an otherwise apparently healthy person is strongly suggestive of sporotrichosis. Tularemia, tuberculosis, syphilis, and staphylococcic infections are usually associated with systemic symptoms. Occasionally blastomycosis, chromoblastomycosis, and actinomycosis will simulate the primary lesion. The diagnosis, when entertained clinically, can be readily substantiated by culture of material from the primary ulceration or an aspirate from a nodule. Characteristic colonies appear from 2 to 14 days after streaking on Mycosel agar.

*Data in Eight Patients with Sporotrichosis**

Case No.	Primary Site	Trauma	Suppuration	Agglutinins	Culture	Duration, Mo.
1	Rt. arm	No	No	..	Positive	2½
2†	Lt. foot	Yes	No	1:160	Positive	6½
3	Rt. arm	No	Yes	1:320	Positive	3
4	Lt. arm	No	Yes	1:80	Negative	3
5	Lt. hand	Yes	No	1:160	Positive	2
6	Rt. arm	No	No	1:40	Negative	1½
7	Finger	No	No	1:160	Negative	4
8	Lt. wrist	No	Yes	1:160	Positive	4

* Skin tests showed positive (+++) results in all patients.
† Lymphangitis occurred in all patients except in case 2.

Our failure to recover the organism in three of the patients was in part related to the inability to secure adequate material because of the various stages of healing induced by prior therapy with iodides. In no patient were we able to demonstrate the organisms on direct smear by Gram's or Gridley's stain. Although lymphangitis appeared in seven of the eight patients suppuration occurred in only three (see table). There was no correlation with duration of illness, site of inoculation, or race. Each patient exhibited a positive reaction to a yeast phase antigen of S. schenckii (provided by Dr. Norman F. Connant, Duke University Medical Center). This reaction has the same significance as the tuberculin reaction, and two of five nurserymen without known infection with S. schenckii reacted to the antigen. The agglutinin levels (see table) were strikingly elevated in all patients tested. Serums from five asymptomatic nurserymen exhibited titers of 1:10 to 1:80. Tests with control serum from our laboratory showed negative results.

The rarity of sporotrichosis in Florida[3] and its prior absence in these nurseries suggest that the fungus is not endemic in these areas. The sudden appearance of this outbreak coincidently with the introduction of sphagnum moss from a new source in an endemic area suggests the possibility that this moss is the vehicle for S. schenckii. Each of our patients had intimate contact with the sphagnum moss, which has been implicated in a previous report.[3] The difficulties encountered in culturing this fungus from the moss have been noted. Although we were unsuccessful in recovering the fungus from the suspected source the speculation that these patients acquired their infections from contact with this moss seems plausible.

Treatment

Various agents have been used in the treatment of this disease, but none have proved superior to or as specific as iodides in adequate doses. The mechanism of its action remains unknown. Large doses of iodides of 4 to 6 Gm. daily will readily control the infection in six to eight weeks. It is recommended that they be continued for another month after complete clinical remission.[1a] Occasionally iodism is encountered, but it can be controlled by discontinuing the drug therapy and restarting at a lower dosage with gradual increase until full therapeutic doses are again attained. The protracted illnesses in some of these patients seem to be related to failure of the patient to take his medicament continuously and to inadequate dosages of iodides.

Summary

A simultaneous outbreak of eight cases of sporotrichosis occurred in two separate forestry nurseries at a time when they both began to get sphagnum moss, which has been previously implicated as a vehicle for S. schenckii, from a new source. Seven of the eight patients had the localized lymphangitic type of sporotrichosis. Trauma was directly implicated in only two. Iodides are specific and will control the infection in six to eight weeks.

Dr. C. G. York of Lake City, Fla., gave permission to study the patients in cases 3, 5, 7, and 8. K. Brown and R. Hay of the Department of Medical Illustrations assisted with photographic work.

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SEXUAL ACTIVITIES AND ATTITUDES IN OLDER PERSONS

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Recognition of the behavioral and physical factors that accompany aging is mandatory if the medical profession is to offer optimum care to an aging population. Sexual activity in older persons is one physiological function about which there is much myth, superstition, and guilt. Information based on hearsay and perhaps dictated by younger members of this society has tended to paint a picture of an asexual adjustment for the older person. The sexual activities and attitudes of 250 volunteer geriatric subjects were assessed as part of an extensive evaluation of the aging process. Despite prevalent notions that older people have no sexual activity, over one-half (54%) of those persons who were married were still active sexually. Sexual interest and activity decline with advancing years, but cessation of sexual activity in the oldest subjects was often found to be related to decline in physical health of one or both of the marital partners.

Recent emphasis in medical education has stressed the need for greater understanding of human behavior. This broadening scope of knowledge is of practical use to the physician in making possible more comprehensive care of his patients. With a rapidly growing geriatric population to attend, the physician of today needs more knowledge of what is ordinary or usual in the life of the older person. Little has been reported concerning the sexual activity and attitudes of older people. There have been many misconceptions, certainly, about the role of sex in the lives of older people in our society. One commonly recognized belief among younger people in our society is that older persons, especially grandparents, have no sexual feelings. As we now recognize, the feelings and attitudes of people are directly related to the expectations of the society in which they live. Thus, it is common for the physician to see in his daily practice older persons who feel guilty about having sexual feelings; often these feelings are not acceptable to the older person, to the physician, or to other people in the environment in which the older person is living. Guilt or anxiety over sexual feelings may

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interfere with the adjustment of the older person and with his interpersonal relations, among which is the doctor-patient relationship. Guilt or anxiety on the part of the patient may thwart the therapeutic efforts of the physician.

While recognizing that the attitudes of society are slow in changing, we believe that more knowledge of this area of human behavior would serve both the physician and his patient, as well as strengthening their relationship to each other. Kinsey and co-workers[1] devoted only two pages in their study of male sexuality to the specific area of sexual activity in the aging man. Similarly, a single table summarizes their data on the aging woman.[2] Much more information is needed in this area in order to determine the role that sexual activity plays in the life of the older person. It is our purpose then, to present some normative data on sexual activity and attitudes in a geriatric population.

Studies Performed on Persons in Population Studied

- Social history
- Medical history
- Psychiatric evaluation
- Physical examination
- Neurological examination
- Ophthalmological examination, including fundus photographs
- Audiometry
- Electroencephalogram
- Electrocardiogram
- Ballistocardiogram
- Chest x-ray
- Microscopic vascular study of bulbar conjunctiva
- Laboratory studies
  - Urinalysis
  - Complete blood counts
  - Nonprotein nitrogen determination
  - Blood sugar determination
  - Serologic test for syphilis
  - Serum cholesterol level determination
- Full-length photograph against grid
- Psychological test data
  - Wechsler Adult Intelligence Scale
  - Rorschach

Materials and Methods

Since 1953, a continuous interdisciplinary study of geriatric subjects living in the Piedmont area of North Carolina has been conducted by members of the Duke University Department of Psychiatry. Each subject has been studied for two days, or about 16 hours. The table contains a complete list of the studies performed on each person. The data on sexual activity and attitudes are but one part of the medical and psychiatric history in this study and, as such, have always been obtained by a psychiatrist member of the research team. All subjects in this study were volunteers from the community in and around Durham, N. C. None of these subjects was hospitalized or living in nursing homes or homes for the aged, and they represent, as a group, a generally successful adaptation to aging. Subjects ranged from 60 to 93 years of age, with an average of 70 years. The study included both caucasoid and negroid men and women. A total of 250 subjects were included in this study.

Results

One hundred one subjects of the original 250 were either single, divorced, or widowed, the greatest proportion of these being widowed. Of these 101 subjects, only 7 reported any sexual activity; thus about 7% of this group were sexually active. The remaining 149 subjects were still married and living with their spouses, and of these, 81 or 54% indicated that they were still sexually active to some degree. Subjects with any degree of regularity and periodicity of sexual intercourse were included in the group called "active." Frequency of sexual relations for the persons in this group ranged from once every other month to three times weekly. Figure 1 indicates correlation of sexual activity with age. Statistical tests of significant differences (chi-square test) indicate that only the fourth group, consisting of those persons 75 years of age or older, showed a significantly lower level of sexual activity.

In figure 2 the sample of married subjects is divided by race, sex, and socioeconomic status. Inspection of these data shows that in this sample, the negroid subjects were sexually more active than the caucasoid; men more active than women, and persons of lower socioeconomic status more active than those of high socioeconomic status. The differences shown in these three bar graphs are valid differences by the chi-square test. We would like to point out, however, that there may be "cross-contamination," so that one variable may influence another; i. e., most of our negroid subjects were also of lower socioeconomic status. Thus the graphs are descriptive of our total sample but should not be taken as independent variables related to sexual activity.

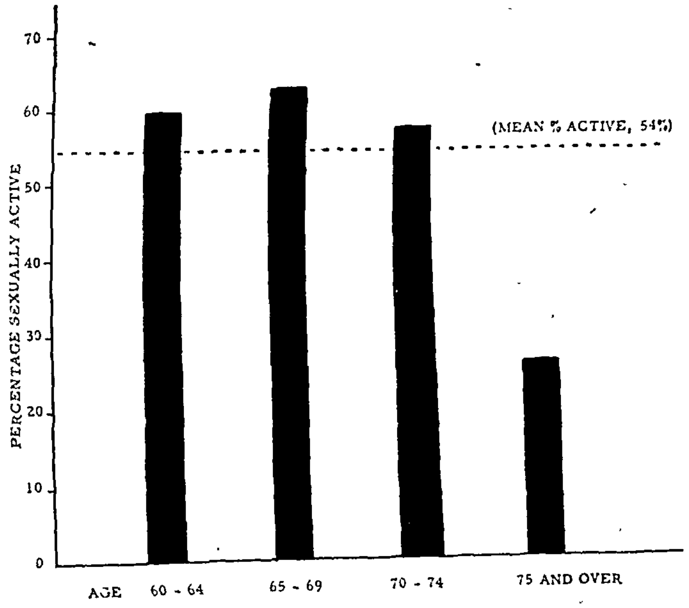

Fig. 1.—Sexual activity related to advancing age in 149 married subjects.

During the interview, each older person was asked to compare the subjectively felt strength of the sexual urge at the present time with its strength in youth. Without exception, every subject rated the strength of the sexual urge as lower in old age than in youth. However, those who rated their sexual urges as strongest in youth tended to rate them as moderate in old age; most persons who described their sexual feelings as weak to moderate in youth described themselves as being without sexual feelings in old age.

Comment

The great difference between 7% of subjects sexually active in the group of single persons as compared to 54% of subjects sexually active in the married group confirms the great influence that marital status has on sexual activity, as pointed out by Finkle and co-workers.[3] This difference is indicative of the gradual lessening of the sexual drive with increasing age; in the absence of a socially sanctioned or legally approved sexual partner, i. e., spouse, the sexual drive, although present, is not often strong enough to cause the elderly person to seek an extramarital sexual partner.

The abrupt lessening of sexual activity in the group of persons aged 75 years and older deserves comment. Many subjects in this segment of our sample had chronic illnesses such as arthritis, arteriosclerotic heart disease, and diabetes. Persons in this group also frequently reported such illness in their spouses. We have consistently found that chronic illness places limitations on all the activities of these persons, although there is an obvious variation in the degree of limitation which depends on the severity of the illness and the subject's attitude toward it. Thus, it was not uncommon for a person of this age group to indicate the presence of sexual feelings in the absence of any sexual activity. These subjects usually stated that sexual activity was stopped because of poor health either of themselves or of their spouses.

The fact that the women in our sample reported less sexual activity than the men also deserves comment, since all persons in this group were still living with their spouses and therefore had adequate opportunity for sexual expression. The possibility exists that the women were somewhat more reluctant to give factual data about their sexual activity; however, we have generally felt that the data obtained in the face-to-face interviews have been reliable. We can point to one factor which may tend to explain this difference, which is that, while the average age of both men and women in this study was about 70 years, the men, by virtue of a trend to marry younger women, and conversely the women, marrying older men, were subjects who were individually reporting on sexual activity in marriages of significantly different age groups. For both males and females in our study, husbands were an average of 4 years older than wives. Another way of saying this is that our "average" male subject aged 70 had a 66-year-old wife, while our "average" female subject aged 70 had a 74-year-old husband.

Conclusions

In a comprehensive, interdisciplinary study of geriatric subjects living in the Durham, N. C., community, data have been gathered and assessed regarding the sexual activity and attitudes of older people. Subjects averaged 70 years of age and ranged from 60 to 93 years. The study included both caucasoid and negroid men and women. Analysis of these data shows little correlation of sexual activity with age, but in this study, negroid subjects were more active than caucasoid and men more active than women. The subjects also rated themselves on the relative strength of their sexual urge in youth and in old age, and a comparison of the two ratings shows a remarkable constancy of the experiencing of the sexual drive within individual persons throughout life. Although older people experienced a decline in sexual activity and strength of sexual drive, these data show that, given the conditions of reasonably good health and partners who are also physically healthy, elderly persons continue to be sexually active into their seventh, eighth, and ninth decades.

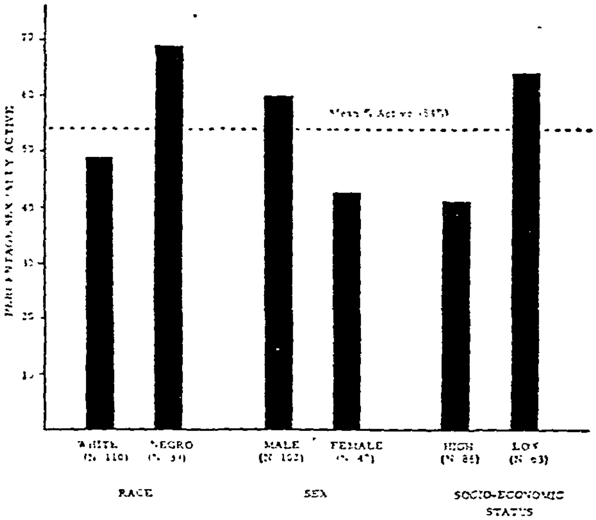

Fig. 2.—Sexual activity related to race, sex, and socio-economic status in 149 married subjects aged over 60 years.

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J.A.M.A., May 7, 1960

PRACTICAL USE OF HYPOGLYCEMIC AGENTS

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The cornerstone of all proper treatment of diabetes mellitus is a diet adjusted to the patient's weight, height, sex, physical activity, and diabetic status. Regular insulin is essential in treating acidosis and coma; the lente insulins and other derived insulins can be used advantageously in combination with it. he group of sulfonylureas which includes carbutamide and tolbutamide must still be used with caution but are known to give the best results in the nonketotic, asymptomatic diabetic whose weight is normal, age over 40 years, and insulin requirement less than 40 units per day. The group of biguanides is represented by phenformin (DBI, phenethylbiguanide), which has replaced as much as 70 units of insulin daily in one patient and promises to play a role not hitherto filled by diet, insulin, or sulfonylureas.

With the advent of multiple hypoglycemic agents, there has been a radical change in the approach to the treatment of diabetes and perhaps considerable confusion in the mind of the average physician as to the proper course to pursue. There is already evidence that administration of these agents may not be the best treatment available for the individual patient. It would seem advisable to attempt some evaluation of hypoglycemic agents and attempt to assign them their proper role in the light of our present knowledge even though, in the case of some of the newer agents, this admittedly is still inadequate.

Diet and Insulin

One can first mention a diet properly correlated to the patient's weight, height, sex, physical activity, and severity of the diabetes. When this diet has been adhered to for a period of time, and assuming that severe acidosis is not present, it is remarkable how many patients require no further hypoglycemic agent. This is the cornerstone of all proper treatment and is being neglected by many physicians for easier methods.

If this measure fails to obtain satisfactory fasting and nonfasting blood sugar levels, that is, good control, then our second most important weapon is insulin. Here only a few points will be covered. It is as important to avoid overdosage and hypoglycemia as it is avoid underdosage and glycosuria and acidosis. Results of the improper use of protamine zinc insulin some 20 years ago in truly labile diabetics can now be seen. Consequently, it is of interest that some of our present work indicates that the duration of hypoglycemia is the most significant factor in producing cerebral cell damage, the severity second, and the frequency of reactions of least importance.

Today there are a number of useful insulins available. Regular insulin is essential in the treatment of acidosis and coma and may be used advantageously in proper combination with protamine zinc insulin. It must be remembered that we are dealing with an unsaturated insulin, or with isophane (NPH) and globin insulins which are saturated, that is, which will reflect all of the regular insulin effect. The lente insulins have proved a worthwhile addition to our armamentarium, and the proper use of the lente triad as described by Whitehouse and others[1] affords a homogeneous mixture which may be tailored to the patient's needs. It is not advisable in the average case to use more than 60 to 70 units of any insulin or mixture in one dose in regular treatment; diabetes in most juveniles is best controlled on two doses daily, about two-thirds before breakfast and one-third before the evening meal. In patients in whom the disease is difficult to control, as the unstable and the truly labile, better results may be obtained by adjusting the evening dose according to the sugar level of the predinner urine specimen. For example, 30 units of insulin should be given if the sugar level is 4+ or 3+, 26 units if the level is 2+ or 1+, and 22 units if the result is negative. Many reactions will be avoided in this manner.

In connection with the administration of insulin, there has been a revival of interest in the jet administration method first described in 1950.[2] In the ensuing years a small group of patients (about 20) have continued to take their insulin in this manner. Most of them have been blind persons unable to use the syringe method or persons with lipodystrophy who were able to avoid this complication by jet injection. While this mode of treatment has been a disappointment due largely to inability to obtain consistently satisfactory instruments, it is again being proposed as an available substitute for syringe injection. While in the ensuing years many of the patients for whom this instrument would have been of value have had satisfactory results with orally given drugs, it is still possibly of potential value, particularly in juvenile diabetes.

Orally Given Sulfonylurea

In recent years a third measure has been available in use of orally given hypoglycemic drugs. The first such drugs to be introduced in the United States were carbutamide and tolbutamide (Orinase).

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CLINICAL NOTES

RECURRENT BACTERIAL ENDOCARDITIS AND AORTITIS WITH RUPTURE OF AORTA

REPORT OF A CASE WITH DEATH FOUR YEARS AFTER INSERTION OF A HUFNAGEL VALVE

Leonard A. Kleinman, M.D., Garfield Heights, Ohio

A 40-year-old man was admitted to the Suburban Community Hospital in Cleveland, Ohio on March 3, 1959, complaining of chills, fever, and hiccoughs occurring during the previous 36 hours. His history of rheumatic fever started at 13 years of age, when the original valvular damage occurred. He had bacterial endocarditis in October, 1948, when he was admitted to another hospital with fever, systolic murmurs heard at the mitral and aortic areas, and an enlarged heart. Cultures of three successive blood specimens were identified as containing Streptococcus viridans. He was treated for one month with intramuscular injections of penicillin, and apparently the infection was eradicated. He remained well until 1953 when cardiac failure developed. When administration of medicaments was no longer effective in maintaining adequate heart function, in 1955 he was referred to the Georgetown University Hospital as a candidate for aortic plastic valve correction of aortic insufficiency. Dr. Charles Hufnagel performed the operation, placing the valve in the proximal portion of the descending aorta. The condition of the patient returned to almost normal but he continued to take digitalis, penicillin prophylactically, and, on occasion, mild sedatives. He remained well until the present illness, with enlargement of the liver persisting as the only sign of cardiac insufficiency.

On examination at the time of admission to the hospital, his condition was toxic and he was acutely ill, with a temperature of 106.8 F (41.6 C), a pulse rate of 100 per minute, respiration rate of 30 per minute, and blood pressure of 200/0 mm. Hg. The clicking of the plastic valve and singultus made auscultation of the heart difficult, but systolic and diastolic aortic murmurs and an apical systolic murmur could be heard. The lower border of the liver was palpable 6 cm. below the right costal margin, but existence of an enlarged spleen was questionable. There were two small lesions on the plantar aspect of each foot resembling petechiae. The neck was slightly rigid. Reflexes and lumbar puncture findings were normal. Results of laboratory tests gave the following information: hemoglobin concentration 12.3 Gm. per 100 cc.; hematocrit value 40%; and white blood cell count 21,000 per cubic millimeter, with a differential count of 89% polymorphonuclear cells, 10% lymphocytes, and 1% monocyte. Serum electrolyte levels were as follows: calcium, 7.4 mg. per 100 cc.; chloride, 95 mEq. per liter; potassium, 3.7 mEq. per liter; and sodium, 123 mEq. per liter. The serum glutamic oxalacetic transaminase (SGO-T) level was 95 units. The blood urea nitrogen level was 31 mg. per 100 cc., with a blood sugar level of 84 mg. per 100 cc. Results of urinalysis showed the pH to be 5.0, specific gravity 1.033, albumin content 4+, a trace of sugar, 3 to 4 white blood cells per field, 5 to 10 red blood cells per field, and many fine granular casts.

A roentgenogram of the chest indicated total cardiac enlargement. An electrocardiogram showed left ventricular hypertrophy and the effects produced by digitalis.

Treatment was started with daily administration of 50 million units of aqueous penicillin, given intravenously, with intramuscular injections of streptomycin and erythromycin. Supportive therapy consisted of administration of fluids and digitoxin. The first blood culture report showed hemolytic Staphylococcus aureus, which was resistant to penicillin and sensitive to chloromycetin, erythromycin, and vancomycin. The administration of penicillin was discontinued and replaced by that of vancomycin. On the fourth day the patient appeared to be semiconscious, rales were heard at the base of the left lung, the abdomen became distended, and edema developed in the legs. Digitalization was again accomplished with use of larger doses of digitoxin, hydrocortisone was given intravenously, and kanamycin was added to the antibiotic regimen. The next day an amazing change took place. The patient was afebrile and alert and his respiratory and pulse rates were normal. Administration of hydrocortisone was discontinued after the second day, but all antibiotic therapy was continued. Blood chemistry reports were normal except for the blood urea nitrogen level, which was elevated to 84 mg. per 100 cc. Results of blood cultures were negative, and it appeared that the patient was recovering.

On the 10th hospital day he had, with sudden onset, chest pain, cough, and cyanosis. Moist rales were heard in both lungs, and a roentgenogram of the chest showed infiltration of the left lower lung.

Carbutamide was found to have a relatively high evidence of side-effects and its use was discontinued. Tolbutamide is still widely used. Later chlorpropamide (Diabenese) was introduced. Recently another drug, metahexamide, was extensively studied, and while it was perhaps the most effective of those discussed, it was abandoned, at least for the present, because of an unexpected occurrence of late hepatic effects. These drugs belong to the sulfonylurea group and seem to act by stimulation of the beta cells of the pancreas to produce further insulin.

Other mechanisms of their effect have been claimed, such as decreased hepatic glucose output, but it has been recently shown that this is also an insulin effect. Sulfonylureas are not effective in depancreatized animals, or human beings, or in the juvenile diabetic with a severe case. If we eliminate cases of poor control due to the presence of intercurrent infections, poor patient cooperation, injections into areas of lipodystrophy, etc., the sulfonylureas have not shown any effect on the truly labile diabetic. However, Fajans and Conn [3] have shown that in the very early and mild stage of diabetes in juveniles, sulfonylureas are effective and may to some degree delay or possibly abort the usual more severe type.

Details of dosage are well described in many sources. It should be noted that equivalent sulfonylurea blood concentrations are obtained by a dose of chlorpropamide that is one-sixth the size of the dose of tolbutamide or carbutamide and about one-tenth the size of the dose of metahexamide. At present tolbutamide is the most commonly used oral hypoglycemic agent. Experience with this drug has been summarized by Moss and others,[4] who reported that of 200 patients with diabetes 49% obtained a good or excellent result, 16% a temporary beneficial effect with a secondary failure, 18% poor results, and 17% no demonstrable effect. As suggested by previous reports they stated that best results could be expected in the nonketotic, asymptomatic diabetic of nearly normal weight, over 40 years of age, and taking less than 40 units of insulin daily.

Phenformin

One other orally given hypoglycemic agent, phenformin (DBI), which is not a sulfonylurea but a biguanide, has been made available. This drug is remarkable as it has replaced as much as 70 units of insulin daily and so far has shown little, if any, laboratory side-effects. In our patients, it has reduced the insulin requirements of the truly labile diabetic by 10 to 50%. Its apparent site of action is in the enzymatic cycle, and it is claimed that it increases the peripheral utilization of glucose. Although some insulin must be present in the body and thus is not effective in the depancreatized person, phenformin would seem to be significant as it has a role that is not fulfilled by diet, insulin, or sulfonylureas in the truly labile diabetic, and it is useful as an adjunct to insulins of other types. Recently two patients with secondary sulfonylurea failure have shown an excellent response to a combination of sulfonylurea and phenformin. Both patients had consistently refused to take insulin. In our experience phenformin has also been reasonably satisfactory in the treatment of mild stable diabetes in adults, in whom the results are similar to those obtained with the sulfonylureas, with the added assurance that secondary failure is unlikely to occur with the biguanide.

Phenformin may produce severe gastrointestinal distress and hence cannot be used by some patients and can be used only in relatively small dosages by others. It is stated that such cases number some 5 to 7%. In our group this figure has been somewhat higher, possibly because of the larger dosage used, although our maximum has been 200 mg. daily. The cause is not local gastric irritation but central nervous system effect. This may often be obviated by use of split dosages, time-release tablets, and by drugs combating the cerebral effect. Because of its unique role in diabetic therapy, phenformin may prove to be of considerable importance.

Comment

It should be stressed that with multiple hypoglycemic agents available, it is increasingly necessary to study and evaluate each case of diabetes as completely as possible so that the proper hypoglycemic agent or combination of agents may be used. The long-term effect of the various orally given agents remains to be evaluated, and if the work of the Toronto group [5] with sulfonylureas and the histopathologic studies of numerous others are verified, later toxic effects are quite possible. It is not important in most cases of diabetes that patients can be kept from severe glycosuria and acidosis by the use of orally given hypoglycemic agents, but it is important that each patient receive the hypoglycemic agents that will most closely restore normal physiology in his particular case.

3919 John R. St. (1).

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rosacea, who were particularly responsive to the hydrocortisone preparation. Sixty-five were definitely improved, four were slightly improved, and five were not helped. Twelve patients using the plain drying agent and eight using that containing hydrocortisone complained of irritation characterized by excessive dryness. Thirty patients using the plain and 21 using that with hydrocortisone complained of slight irritation. This was controlled by discontinuing the drying agents for a few days. In most cases, resumption of application of the medicaments was not accompanied by further irritation, indicating a "conditioning" of the skin.

Comment

The results compiled by each author were similar to those of the others and infer reliability of the clinical impressions reported. It was observed that the best results with these drying agents were obtained in those patients who had unusually severe oiliness of the skin. Conversely, blond patients with thin skin which was not too oily experienced the less favorable results and most of the irritating reactions.

We observed that complaints of excessive dryness from use of the medicaments could be minimized by proper instruction of the patient. This is important, since these drying agents are markedly active and should not be applied as often as is usual with "acne drying lotions," particularly when strongly drying surfactant cleansers are used for therapeutic washing of the skin. At the start all patients were instructed to apply the medicament once daily. Boys preferred to make this application at bedtime. Girls could use it this way or in daytime as a make-up base. A thin film matches blond skin while heavier films suit brunets better. If after one week the skin was not sufficiently dry, the number of applications was increased to two and rarely to three a day.

It is a common observation that even in acne patients certain areas of the face are less oily and dry more readily than other areas. This is particularly true of the nasolabial folds and the angles of the mouth. The drying agents should be kept away from these areas. When they are used more than once daily, the second application can be limited to the lesions, without spreading the film over the entire face.

Summary

Two new topical agents which dry, peel, and degerm effectively the skin of patients with acne were tested clinically. One contains 0.25% hydrocortisone. Their marked drying activity appears to be due to synergism between the contained sulfur, calamine powders, and a new nonionic surfactant, polyoxyethylene lauryl ether. This drying surfactant appears to have properties similar to those of resorcinol. However, it has the decided advantage of not sensitizing or staining the skin.

The use of these drying agents, as adjuncts to the usual therapeutic routine, resulted in improvement of acne lesions in 873 of 909 patients. The preparation containing hydrocortisone was particularly effective in the patients with acne rosacea and in those with acne exhibiting marked erythema.

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Bacteriological evaluations were performed by W. I. Metzger, Ph.D., Chief, Bacteriology Department, Cook County Hospital, Chicago.

The acne drying agents (Fostril Lotion and Fostril HC Lotion) were supplied by Westwood Pharmaceuticals, Buffalo 13.

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INCREASING EXPOSURE TO ESTROGENS.—Tariff Commission Reports does not list the amount of diethylstilbestrol manufactured in the United States as a separate item, but our own experience and knowledge of other major manufacturers in this field lead to an estimate of 10,000 pounds or more per year. As an increasing amount is being used in animal husbandry, the number of those exposed must be increasing at a rapid rate. . . . A review of the world literature shows that since 1941 the absorption of diethylstilbestrol by chemical workers has been a problem everywhere. More recently, the use of this chemical in animal husbandry has increased the number of people exposed. . . . Unexposed chemical workers excreted estrogens below the threshold of the test (0.02 micrograms per ml. of urine). Exposed and imperfectly protected workers showed values ranging from 0.06 to 0.55 μg/ml. Earliest symptoms of breast stimulation were seen one to two weeks after urinary excretion reached or exceeded 0.1 μg/ml.—R. M. Watrous, M.D., and R. T. Olsen, B.S., Diethylstilbestrol Absorption in Industry: A Test for Early Detection as an Aid in Prevention, *American Industrial Hygiene Association Journal*, December, 1959.

POSTOPERATIVE ARTERIOVENOUS ANEURYSM IN MESENTERY AFTER SMALL BOWEL RESECTION

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An abdominal exploration for an arteriovenous aneurysm in a 34-year-old woman revealed such a lesion to be present in the mesentery of the small intestine. This lesion apparently occurred after resection of the small bowel which was performed for intestinal obstruction secondary to adhesions and associated with gangrenous bowel with mesenteric thrombosis. The arteriovenous aneurysm was situated in the healed mesenteric suture line near the base of the mesentery. Excision of this portion of mesentery was followed by uneventful recovery, with complete relief from abdominal pains and recurring mild diarrhea. A review of the literature on gross arteriovenous aneurysms reveals postoperative arteriovenous aneurysms to have occurred in the operative site after various operative procedures, as a direct result of the technical management of the contiguous artery and vein. These procedures have been reviewed, in their case reports, by Elkin and Banner[1] and most recently by French and coworkers,[2] and include blood letting, thyroidectomy, insertion of Steinman's extension pins, amputations, fasciotomy, nephrectomy, radical mastectomy, hysterectomy, intervertebral disk removal, and thoracentesis. An arteriovenous aneurysm occurring in the mesentery of the small intestine either spontaneously or postoperatively has not, however, been previously reported and provides the reason for this report. This additional location further emphasizes the diversity of its possible locations and the diagnostic challenge presented by all persons with complaints who have had operative procedures, because of (1) its variability of symptoms relative to location—local and systemic circulatory effect and (2) the variability of the time elapsed since the operations. It emphasizes the clinical importance of seeking out bruits and thrills over regions of surgical scars.

Report of a Case

A 34-year-old married woman was admitted to the Norwegian-American Hospital on July 15th, 1952. In March of that year she had had, at another hospital, a resection for intestinal obstruction as a result of adhesions and complicated by gangrenous small bowel (near the terminal ileum) and mesenteric thrombosis. For several hours prior to the operation she complained of severe abdominal pain. The record revealed that on opening the abdomen there were loops of gangrenous ileum, near its terminal portion, associated with thrombosed mesenteric vessels, and free, dark blood in the peritoneal cavity. Adhesions and a cecum adherent to an old McBurney's incision scar were freed. The gangrenous portion of the ileum and its attached mesentery were resected, and continuity was established by an end-to-end anastomosis near the terminal portion of the ileum. The uterus was noted to be three months pregnant. A spontaneous miscarriage occurred a few days later, requiring a dilation and currettage. The patient was discharged several days later, complaining, however, of vague abdominal pains and mild diarrhea. One week later, on March 28, 1952, the patient was admitted to a second hospital at 2:30 a. m. for pain in the right lower quadrant that had suddenly begun that evening. Since dismissal from the first hospital, the previous week, the patient continued to have mild diarrhea. Physical examination at the second hospital, according to the record, revealed a distended abdomen, a midline subumbilical incision scar, tympanic abdomen but without audible bowel sounds, and a strong systolic murmur in the right lower quadrant. Laboratory findings were normal. The patient was dismissed two days later. Subsequently she was also admitted to a third hospital for several days, without receiving specific treatment, before coming to the present hospital, the fourth.

Her complaints now, in July 1952, were chiefly vague abdominal pain and mild recurrent diarrhea. A continuous, loud, and roaring murmur with systolic accentuation was heard over the right lower quadrant of the abdomen. There was no palpable mass nor tenderness in the abdomen. A diagnosis of an arteriovenous fistula in the abdomen was made, but without further specific localization. In addition, a right paramedian abdominal incisional scar and a McBurney's incision scar were found. The pulse rate was 80 per minute and regular, and blood pressure was 110/70 mm. Hg. Results of serology were negative. Hemoglobin determinations varied from 12.8 to 16.1 Gm.% and from 84.5% to 106 Gm.% respectively. The leucocyte count was 16,000 per cubic millimeter on admission but subsequently fell to 6,500. The differential white blood cell count was 66% of segmented polymorpho-

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nuclear leucocytes and 34% lymphocytes. The urine was acid, with a specific gravity of 1.036. The blood type was O, Rh-positive. An aortogram visualized a normal aorta, inferior mesenteric and external and internal iliac arteries, and proximal parts of the superficial and deep femoral arteries.

Abdominal exploration revealed a continuously, coarsely, and rapidly vibrating, thickened area in the mesentery of the small intestine near its base, in the suture line scar of the mesentery from the previous intestinal resection. This vibrating mesenteric area was observed to be thickened partly because of edema, particularly at the base, and the edema extended peripherally along the mesentery to the intestinal wall. The vessels appeared engorged. Because the mesenteric vessels consist of several arcades at this level, the vibrating mesenteric area was simply resected between multiple clamps and the opening in the mesentery closed. The bowel appeared as pink after resection of this area of mesentery as before. The patient made an uneventful recovery and subsequently did not suffer abdominal pain nor episodes of diarrhea for as long as several years later.

The removed section of mesentery is shown in figure 1, with a match stick in the artery pointing to the aneurysmal dilatation. Also, the aneurysmal dilatation can be observed to be continuous with the vessel with a larger lumen, the vein, adjacent to it. This may be better observed from the operative specimen photographed under water (fig. 2).

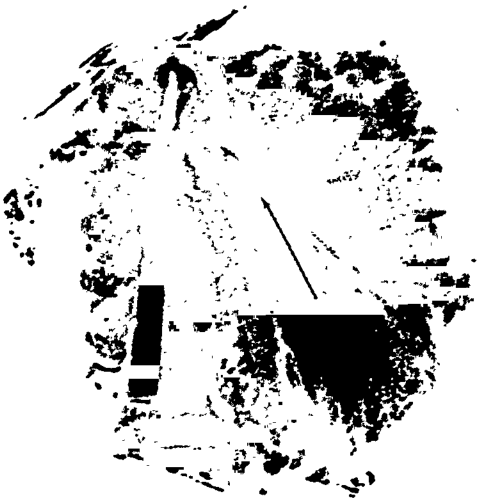


Fig. 1.—Match stick inside arterial lumen pointing into aneurysmal dilatation. *Arrow*, inside opened vein, leading into same aneurysmal dilatation; surrounding area is mesenteric fat.

Summary and Conclusions

A case of arteriovenous aneurysm of the mesentery of the small intestine is reported for the first time. This followed a resection of the small intestine by a short interval and occurred in the suture line of the mesentery, near its base. Its occurrence should not be entirely unexpected, since arteriovenous fistulas or aneurysms at the operative sites of various surgical procedures have been reported.

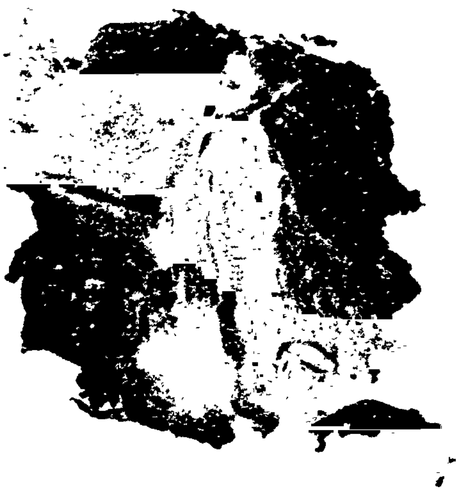


Fig. 2.—Photograph of specimen under water originally in black and white, with *arrows* in the two vessels leading to aneurysmal dilatation; long *arrow* inside vein.

From the variability of the cases and of the surgical procedures which have led to its formation, from the varying symptoms and signs compared with other reported cases, and from the varying time interval before appearance of symptoms, the clinical points that appear pertinent are as follows: 1. Careful attention to the separate management of contiguous arteries and veins should be exercised, if possible and feasible, to prevent an arteriovenous fistula or aneurysm. 2. Careful venesection, avoiding the thrust of the needle completely through the vein into an adjacent artery, should be practiced and similar caution to avoid puncturing both the artery and vein in the process of percutaneous arteriography should be exercised. 3. Operations performed even many years earlier may possibly be considered responsible for the symptoms and signs of arteriovenous aneurysm in the vicinity of the operative region because of the varying interval from the operative procedure to the formation and clinical manifestations of the arteriovenous fistula. 4. The symptomatology may vary with the region of the body involved, and, as is well known, with the size of the fistulous communication and with its distance from the heart.

Table 1.—*Drugs Which Stimulate and Depress, Showing Beta Pattern Activity*—Continued

Drug	Action	Reference
	Local Anesthetics	
Cocaine	Excursions of frog heart; turtle heart; tonus of esophagus, stomach, colon	Sollmann,[10] pp. 270-271
	Drugs Acting on Autonomic Effector Cells	
Acetylcholine	Skeletal muscle*	Goodman and Gilman,[8] p. 601
	Crawfish heart*	Sollmann,[10] p. 199
	Human heart*‡	Sollmann,[10] p. 335
Neostigmine	Autonomic ganglions; skeletal muscle*	Goodman and Gilman,[8] p. 450
Physostigmine	Skeletal muscle*‡	Goodman and Gilman,[8] p. 446
	Respiration†‡	Goodman and Gilman,[8] p. 447
Diisopropyl fluorophosphate	Respiration†‡	Goodman and Gilman,[8] p. 460
Epinephrine	Coagulability of blood	Sollmann,[10] p 371
	Contractions of dog uterus‡	Sollmann,[10] p. 375
Phenylephrine	Cat intestine*‡	Sollmann,[10] p. 388
Ephedrine	Myocardium*	Drill,[9] chap. 26, pp. 16-18
	Turtle and rabbit myocardial rate and amplitude	Sollmann,[10] p. 381
2-Methylaminoheptane hydrochloride (oenethyl)	Myocardium*	Drill,[9] chap. 26, p. 24
Betaphenylethylamine	Myocardium and coronary arteries*	Sollmann,[10] p. 386
Amphetamine	Central nervous system‡	Goodman and Gilman,[8] p. 518
	Stomach*‡	Goodman and Gilman,[8] p. 520
Atropine	Smooth and cardiac muscle* and other cells	Sollmann,[10] p. 309
	Tone and peristaltic movements of excised ureter	Sollmann,[10] p. 313
	Structures blocked by atropine‡	Goodman and Gilman,[8] p. 543
	Medulla and higher cerebral centers‡	Goodman and Gilman,[8] p. 544
Levo hyoscyamine	Tone and peristaltic movements of excised ureter	Sollmann,[10] p. 313
Yohimbine	Intestines, bladder, spleen*	Sollmann,[10] p. 278
Nicotine	Sympathetic, and parasympathetic ganglions§‡	Goodman and Gilman,[8] p. 620, Drill,[9] chap. 22, p. 15
	Central nervous system‡	Goodman and Gilman,[8] p. 621, Sollman,[10] p. 341
	Adrenal medulla‡	Goodman and Gilman,[8] p. 621
	Ciliary movement of frog esophagus‡	Sollmann,[10] p. 342
Anabasine	Autonomic ganglions§‡	Sollmann,[10] p. 345
Lobeline	Ganglionic transmission‡	Goodman and Gilman,[8] p. 628, Drill,[9] chap. 22, p. 15
Tetraethylammonium (TEA)	Skeletal muscle*	Goodman and Gilman,[8] p. 630
Tetra-methyl ammonium chloride	Medullary centers (respiration)†‡	Sollmann,[10] p. 340
	Histamine and Its Antagonists	
Histamine	Excised ureter*	Sollmann,[10] p. 411
	Tonus of cat capillaries‡	Sollmann,[10] p. 408
	Uterus*‡	Sollmann,[10] p. 294
Peptone	Uterus*‡	Sollmann,[10] p. 294
Pituitary extract	Uterus*‡	Sollmann,[10] p. 294
	Antiseptics, Disinfectants, and Drugs Used in Chemotherapy of Infectious Diseases	
Quinine	Protoplasmic functions	Goodman and Gilman,[8] p. 1191
	Phagocytosis	Sollmann,[10] p. 506
	Uterine contractions and tonus	Sollmann,[10] p. 510
	Respiration†	Goodman and Gilman,[8] p. 1198
Pamaquine Naphthoate	Uterus*	Sollmann,[10] p. 521
Penicillin	Treponema pallidum	Goodman and Gilman,[8] p. 1236
Emetine	Smooth muscle of digestive tract*	Sollmann,[10] p. 495
Sulfonamides	Excised frog heart*	Sollmann,[10] p. 556
Sulfanilamide	Bone marrow*‡	Sollmann,[10] p. 555
Methylene blue	Intestine*	Sollmann,[10] p. 589
Boron	Growth of beans and flax	Sollmann,[10] p. 601
Iodine	Yeast growth	Sollmann,[10] p. 820
Aspidium (male fern)	Spinal cord‡	Goodman and Gilman,[8] p. 1134
Chenopodium oil (American wormseed)	Central nervous system‡	Goodman and Gilman,[8] p. 1136
Thymol	Central nervous system‡	Goodman and Gilman,[8] p. 1139
Betanaphthol	Central nervous system‡	Goodman and Gilman,[8] p. 1140

* [illegible] or tonus.
† [illegible] me.
‡ [illegible] g is assumed to have increased during time of absorption.
§ Transmission of nervous impulse.

of pharmacology surveyed were those by Goodman and Gilman,[8] Drill,[9] and Sollmann.[10] There are a number of cases in which the effect of the drug under consideration was not fully elucidated. In general, such cases fall into three categories, those involving muscular response; those involving respiration; and those involving transmission of nerve impulses. The assumption is therefore made that the action of a drug unless otherwise stated, is to change the contractility or tonus of muscular tissue, to change minute volume of respiration; or to transmit nervous impulses along or through nerves and ganglions.

Table 1 deals directly with the phenomenon already discussed, namely a stimulation at low levels of a drug which gives a depression at higher concentrations. There are other instances in which substances appear to depress at the lower level and stimulate at higher levels. Others depress, stimulate, and depress again in a sine wave response, eventually terminating with accumulation of toxic concentrations. These are presented in tables 2 and 3 respectively. It is possible that the examples in the second and third tables are simply selected areas in a more complicated dose-response curve.[11] The examples presented are representative and are by no means all of those to be found in medical pharmacology. For example, one could add all stimulant drugs to the list, since in high enough concentrations they become toxic and depress cellular function. Any substance would be harmful in high enough concentration, regardless of its initial effect.

It is important to note that this survey has apparently divided the drugs into four groups according to the response pattern. These patterns are identified for discussion purposes as alpha, beta, gamma, and delta. The alpha pattern is represented by drugs not listed in the tables; these drugs have not yet been shown to give a stimulatory response. If it is possible for them to stimulate, the proper subinhibitory level may not have been tried, or the method of measurement may not have been sensitive enough to record the stimulation. Drugs having beta pattern activity (table 1) show a single peak of stimulation followed by a depression or negative response as the concentration is increased. The gamma (see table 2) pattern shows a depression at the lowest concentration followed by a stimulation. These drugs would all probably show a second depression as do those in table 3 (delta pattern), if the concentration were further increased. It seems probable that the gamma and delta patterns of drug action are part of a single pattern. More than one stimulation peak has been seen occasionally in chicks fed antibiotics and is typical of the response obtained by Richet [7] with heavy metals. These concepts are summarized in the figure.

TABLE 2.–*Drugs Which Depress and Stimulate, Showing Gamma Pattern Activity*

Drug	Action	Reference
Hexobarbital, amobarbital, and pentobarbital	Tonus and rhythmic Contractions in Thiry Vella fistula in dogs*	Drill,[9] chap. 14, p. 7
Apomorphine	Central nervous system	Sollmann,[10] p. 491
Caffeine	Choice (cancellations, etc.)	Sollmann,[10] p. 214
Acetylcholine	Tonus of vessels in most organs Contraction and relaxation of frog skeletal muscle	Sollmann,[10] p. 336 Sollmann,[10] p. 337
Pilocarpine	Turtle esophagus*†	Sollmann,[10] p. 295
Epinephrine	Pregnant human uterus†	Goodman and Gilman,[5] p. 490
Epinephrine, ephedrine, pseudoephedrine	Bronchial musculature†	Sollmann,[10] p. 380
Amphetamine	Excised intestines†	Sollmann,[10] p. 384
Peptone	Excised mammalian heart†	Sollmann,[10] p. 414
Chlorine	Bronchial musculature; rings of pulmonary artery and vein†	Sollmann,[10] p. 151
Cobalt	Peristalsis*	Sollmann,[10] p. 956
Colloid metals	Number of leukocytes*	Sollmann,[10] p. 857
Insulin	*Rabbit's small intestine*†*	*Sollmann,[10] p. 62*

* Concentration of drug is assumed to have increased during time of absorption.
† Changes contractility or tonus.

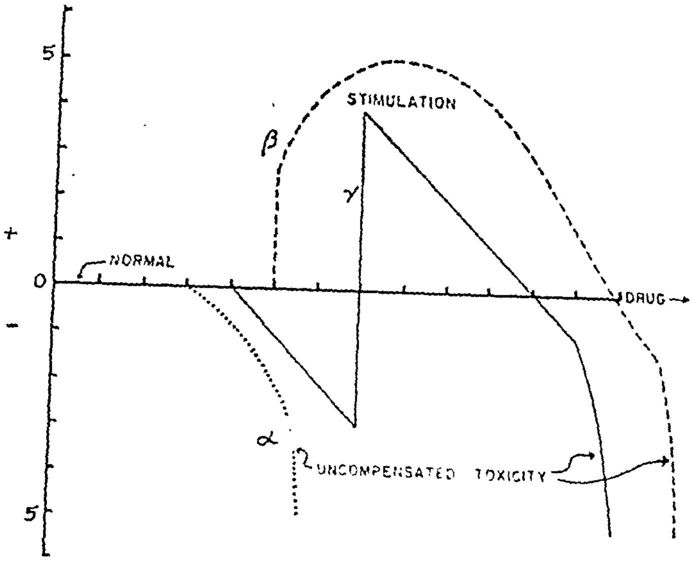
A possible mechanism of action at the cellular level has been suggested [11] as follows: The stimulation reflects limitations in the ability of the organism to equate or modulate its response to a given stimulus at the lowest threshold of perception. If we assume that the response involves a chemical reaction, then the response of the organism is a unit (discontinuous) response, in which the lowest possible reaction would require one or more molecules to be changed. The release of an enzyme, proenzyme, hormone, or ribonucleic acid information molecule could quickly change the internal character of cells. The minimum response is an apparent overcompensation at the sensing threshold of the organism.

TABLE 3.–*Drugs with Sine Wave Dose-Response Curves*

Drug	Action	Reference
Morphine	Tissue edema of addicted rats	Sollmann,[10] p. 251
Sodium Bromide	Cat central nervous system	Sollmann,[10] p. 811
Strychnine	Muscle tonus	Drill,[9] chap. 22, p. 9
	Medullary and spinal functions	Sollmann,[10] p. 198
	Heat regulation	Sollmann,[10] p. 197
Acetylcholine	Respiration*	Sollmann,[10] p. 337
Epinephrine	Perfused frog heart†	Sollmann,[10] p. 369
Calcium	Perfused respiratory center of frogs	Sollmann,[10] p. 786
Tellurium	Blood-forming organs	Sollmann,[10] p. 900

* Changes in minute volume.
† Changes contractility or tonus.

The complexities of higher organisms lead to interactions between different cells and tissues. This allows a more complex reaction mechanism to be visualized. In spite of this, the over-all patterns of response are similar to those seen with micro-organisms. Irrespective of mechanism, common denominators evidently exist in the response of organisms to drugs at the threshold of perception and response levels. Experience with antibiotic stimulation in animals has indicated that the pattern of response is delicately tuned to environmental nuances. Such problems are not seen in this survey; they would have been seen had the survey included exact quantitative data from original literature.



Drug response patterns shown, with units of drug concentration on abscissa and response units on ordinate. Relative position of three curves is without significance. α drugs allow no net positive response, whereas β drugs give stimulation which may or may not be cumulative. Inhibitory action of γ drugs is more than overcome by response of organism. These drugs apparently inhibit below perception-response threshold.

Summary and Conclusions

The fact that so many apparently unrelated stimuli produce the same general response (for example, stimulation followed by depression) at least suggests that there are a few fundamental processes by which the cell responds to all such stimuli rather than myriad processes by which it responds to a wide variety of compounds. The complete spectrum of drug-response patterns should be known. Demonstration of the uniformity of response in the face of diversity of stimulation (hormesis and hormetics are themselves but a small part of the field of hormoligosis) should point the way to a better understanding of drug action and allow some generalization in basic cellular physiology.

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INSECT-VECTORS AND INSECTICIDES.—Physicians have learnt to use antibiotics with discretion to achieve their most important cures and there is some evidence of diminished incidence of resistance in well-conducted hospitals. The situation with insecticide resistance is much less reassuring. The numbers of species of arthropod of public health importance which have revealed resistant strains is now over 50 and is steadily growing. . . . The extreme case of drug-dependence has not been reached with insects. The nearest approach is a suggestion that certain pests (houseflies, bed bugs), having become resistant to dieldrin, are actually more numerous after spraying than before. The only instance in which this has been actually proved is when dieldrin is applied to primitive latrines to suppress fly breeding. This seems to be due to the dieldrin suppressing another type of fly maggot, which normally renders the faecal matter unsuitable for housefly breeding. There are many other reports of similar increases in flies and bed bugs where the dieldrin has been applied only to wall surfaces. These are unexplained at present; but it would be rash to assume that the insecticide was having a direct, beneficial effect.—J. R. Busvine, D.Sc., Fundamental Aspects of Insecticide Resistance, *Pharmaceutical Journal*, Jan. 23, 1960.

SPECIAL CONTRIBUTION

RESEARCH—THE "R" IN NURSING

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"Research in nursing? What is that?" Doctors often ask me this question when I talk about new developments in my profession which we, as nurses, think bear evidence of our deep concern that more and better nursing service reach the patient.

I suspect that the question is often asked in genuine curiosity, but equally often one can detect a hint of skepticism or fear. Not much is said about nursing research outside of the nursing journals and a few social science publications where projects are reported because the aspect of nursing investigated has sociological implications. It is obvious, therefore, that when not much is known about a new and expanding process, it is bound to be suspect or misunderstood. But, while research in nursing is comparatively new, there is a tremendous amount of activity under way, and much thought and imagination are going into the exploration of a wide variety of topics which should be of interest to the medical profession. Perhaps the two points of most immediate interest and concern are these: 1. Nursing research is relatively small as an area of practice for nurses, and few nurses are either qualified or preparing themselves to become qualified in this specialty. 2. It is not drawing practitioners away from the bedside, but it should have the opposite effect; the findings of careful investigations should aid recruitment and add to the attractiveness of patient care.

Nursing research is an outgrowth of the demand for improved health services during the past decade and of the expansion of the nursing profession itself, which in its own coming of age has asked what it can do to give better patient care. Aware that professional status is truly signified by a profession's willingness to assess and improve its practices, nurses have set out to add to the improvement of patient care by acquiring better knowledge of the patient's nursing needs and of themselves. As early as 1949, the *American Journal of Nursing* urged nurses to make plans for scientific investigation. From 1950 to 1955, the American Nurses' Association supported studies of nursing beginning with studies of functions of nurses and branching out to other studies. The ferment of growth and the realization that professional status bears direct relationship to the amount of self-questioning that a profession encourages culminated in 1955 in the creation of the American Nurses' Foundation, a center for research which is largely supported by nurses. The foundation has sponsored research in the areas of practical, industrial, psychiatric, and outpatient nursing and in the care of the chronically ill.

Federal grants and grants for research in nursing from private foundations concerned with mental as well as physical health have also stimulated nurses and others to formulate hypotheses around basic nursing problems. The most significant fact is that nurses themselves have taken the lead in this movement toward self-study and evaluation of function because they could not wait for other disciplines to recognize and examine the many changing and increasing needs of patients with which nurses contend, or by which they are frustrated, 24 hours a day.

Problems Being Researched

What nursing problems are being studied? First, there are the problems of the nurse herself. Who is she? Why did she choose to become a nurse? What does she think? What does she do? What do we as nurses think she should be doing? What preparation or experiences will produce this result? Second, we are looking at nursing procedures, those activities which we define as specifically nursing, to examine them to determine what scientific basis they have. Which ones are effective in terms of patient progress? Are other activities needed to give better nursing care? Which ones are ritual and can be dispensed with? What procedures could be of more assistance to physicians? How can the effective procedures and activities best be taught? The health care area is the third large area. What specific role does the nurse play in the total spectrum of health care? What can she add to total patient care? The fourth area is that of the management of patient care and great variety of personnel. How can nurses work with maximum efficiency in relation to specific patient needs? How can we insure at all times that the patient is the center of the activities?

Nursing research is often multidisciplinary. This is revealing of its humaneness, in the sense that its goal is patient welfare. It cares about people, draws on the skills of many to understand the person within the patient, and seeks to find ways of minimizing pain and speeding recovery.

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The principal investigators or co-investigators of many projects mainly have been nurses, and the next largest group have been social scientists. Project directors have included, among others, physicians, educators, engineers, and hospital administrators. It is significant that a recent publication [1] on some of the findings of studies to date has a professor of sociology as senior author.

Two early projects made notable contributions from 1947 to 1950. The Arnstein-Stobo study leading to "Cost Analysis for Public Health Nursing Services," developed a method for studying costs of public health agency operation. The study conducted by Ole Sand at the University of Washington and reported in the three-volume "Basic Nursing Education, Curriculum Study Series," had as its purpose to re-examine the curriculum of the basic collegiate nursing program to see through what means it could be improved and shortened.

Leo Simmons, at Yale University, reviewed 5,000 documents reporting nursing studies over the past 50 years. This study will be the basis of a forthcoming publication, "Survey and Assessment of Research in Nursing."

Here are some examples of the scope of nursing research at present. Can operations research help us find simpler answers regarding management and staffing predictions in the hospital? Dr. Daniel Howland, Department of Industrial Engineering, Ohio State University, is developing a methodology for evaluating patient care within a hospital in terms of such restricting factors as money, plant, equipment, and manpower. This project uses a number of disciplines beside nursing, such as philosophy, sociology, mathematics, and business administration, and it will encompass a number of smaller studies, such as one based on a psychologist's interviews with diabetic patients.

Which nurses will make good supervisors? Dr. Elizabeth Hagen, Institute of Research and Service in Nursing Education at Columbia University, has been developing instruments for identifying behaviors of nurses who are capable of assuming leadership positions in general hospitals.

Why do students who would make good nurses drop out? Social psychologist David Fox, Columbia University, is identifying stress patterns among student and graduate nurses as related to factors of social background, personality factors, and educational and professional experience.

What problems or needs of patients do public health nurses perceive in their personal contacts with patients? How do they act on their perceptions? Dr. Clara Hardin, American Nurses' Foundation, is studying the dimensions of the public health nurse function, with emphasis on interpersonal relationships between nurse and patient.

How can the nurse better prepare the patient for going home? Marjory J. Hook, assistant professor of nursing, University of Nebraska, is observing problems faced by children when they go home from a psychiatric therapy service and the nurse's role in facilitating return to community living.

How does skilled nursing affect welfare of older patients? Martha M. Brown, nurse educator and clinician, is working at Washington University, in St. Louis, on the repersonalization of older patients. This study, very timely in view of our increasingly aging population, will demonstrate the repersonalization which can take place in the older patient who is provided with expert nursing care.

More physician-nurse joint research is needed. The results would be of value to research and to interdisciplinary relationships in general. Doctors and nurses could put forth more effort in considering the skills of each when designing their research. Three projects are good examples of such research.

A physician-nurse team under the leadership of Dr. Albert Snoke, director of Grace-New Haven Community Hospital, is studying professional activities and relationships of the nurse with other medical personnel, with a view to increasing interdisciplinary participation in planning care. Dr. George C. Reader, director of research, Cornell University Medical College, is co-investigator with Doris Schwartz, R.N., in a study of the nursing needs of chronically ill ambulatory patients. Dr. John Parks, professor of obstetrics and gynecology, George Washington University, and Caroline Russell, R.N., are working to determine the amount and type of nursing service which make the maximum contribution to maternal and infant welfare during the maternity cycle.

Division for Nursing Research in the Public Health Service

The Division of Nursing Resources was created in 1949 as part of the Public Health Service to help solve nursing shortages through survey and research methods. It has undertaken basic and applied research. It has accepted the unique role of being the only federal unit concerned basically with sustaining balance of nurse supply and demand and stimulating and conducting research in all areas of nursing.

Observations have recently been concluded on two projects which will be of interest to doctors. Each was developed under the direction of a nurse-investigator. The purpose of the premature infant study, conducted with the help of nurses at Bellevue Hospital, New York City, was to determine whether a support (a rolled diaper) at the back of a premature infant contributes to weight gain or otherwise affects its development. The history of this study bears telling because it shows how a nurse-scientist develops, how a research question swims into the searching mind, and that research in nursing has application to patients of all ages. The project director had noticed, while she was a head nurse in the premature unit, that "preemies" would wriggle to the end or side of incubators or bassinets. As she went about her work, she wondered why? Was it possible that infants craved extra back support? Might extra support contribute to weight gain? She had a hunch that it did.

Thus from May to November, 1958, 60 premature infants were divided into a control group, which received standard care, and an experimental group, which had the benefit of support. The infants were observed every 10 minutes around the clock for 42 days for details of their sleep-wake patterns, and vocal, bodily, and feeding behavior. We now know how each of these infants behaved, slept, cried, moved about, ate, or gained. This project has given us detailed information on infant behavior, never before recorded, or perhaps known.

The infant study has put this hunch to test. The data are now being analyzed. Whether or not the application of a diaper roll support affects weight gain, this study, which came as a result of a nurse's initiative and creativity, has produced data which can be used by physicians, psychologists, and social scientists. It demonstrates that nursing care can be objectively measured, it has implications for the staffing of premature units, and it is a purposeful step in strengthening nursing practice in premature units against its traditional dependence on trial and error.

As often happens, a unique and unplanned-for by-product of this study was a check list for observation of infant eating behavior. This evolved when the chief investigator realized that terms such as "ate well" or "ate poorly" did not have the same meaning to different nurses or doctors. The check list provided objective criteria for measuring and recording infant feeding behavior for the first time.

Another study in the Division of Nursing Resources raised provocative questions about nursing education. In the study of nursing students' perception of patients' attitudes, about 400 students in seven schools selected the patients whom they knew best and answered questions as they thought their patients would answer. Their patients then responded to the same question. Students knew best the patients who were friendly, cooperative, and cheerful.

Freshmen and seniors had like difficulty in estimating the importance to patients of various aspects of hospital care. When students disagreed with their patients, they were more apt to overestimate the importance of the social environment and to place less value on items relating to physical care, information, and assurance than did the patients. These and other findings should be of special interest to teachers and supervisors who are concerned with patient care and with planning the learning experiences for students. We may arrive at a method of indicating if student nurses need additional help in getting to know their patients. Is modern nursing education as effective in this area as it thinks it is?

Nurse recruitment, comprehensive patient care, and the relationship between theory and practice of nurse supervisors are also under study by nurse consultants of the Division of Nursing Resources.

Earlier Division of Nursing Resources' activities led to the development of methods for bringing more professional nursing care to patients without increasing the number of nursing personnel. These methods have resulted in the production of several manuals to help hospitals effect economies along with improvement of nursing services—"How to Study the Nursing Service of an Outpatient Department," "How to Study Supervisor Activities in a Hospital Nursing Service," and "How to Study Nursing Activities in a Patient Unit."

Preparation of the Researcher

In nursing, the scarcity of prepared investigators is greater than in most other fields. Research in any field requires a certain amount of specific preparation and discipline. To date, much of the research carried out in medicine and nursing has been done by specialists who may not be doctors or nurses but who may be biochemists, pathologists, or social scientists. While it is true that today research has "band wagon" status in all areas of learning, this should not distress us. The publicity will stimulate those with good potential to enter the field; those who have not the capacity for development will soon divert their energies elsewhere when they experience the rigorous discipline of research methodology.

Nursing is just beginning to prepare a few of its members to become investigators. It is a long, slow process, and the selection of good candidates is difficult. Often we are asked how nurses are being prepared for research and how many are needed. Education for research involves the same arduous effort and time for nursing as for other disciplines. There are no short cuts, and nurses who hope or believe they can become investigators without solid preparation on the graduate level will be doing themselves and their profession a disservice. Only a few professional nurses in comparison with the total number currently active will be needed, and only a few will be capable of developing the special skills required for scientific study. Only a few of our 460,000 nurses who are now practicing will be temperamentally suited to research careers. But we hope that the efforts of these few will increase the effectiveness of all levels of nursing personnel: the professional, the practical nurse, the aide, and the orderly, for the aim of all our studies is in the long run, to produce better patient care.

Our profession faces a few major problems in its efforts to develop nurse-investigators. Our advanced nursing education programs need to develop content specifically aimed toward qualifying those who want to pursue careers in research. This is being done by joint planning and joint programs with basic and social science educational institutions offering graduate work geared toward research. At present, several nurses are working for doctorates and are learning research methodology in some of the universities in departments of the various basic and social sciences. After completing the degree requirements, they intend to apply their knowledge in the field of nursing research.

A second need is for better-prepared faculty to staff graduate programs in research methodology. Some of us would like to see opportunity and time provided to the instructors in graduate programs so that they may engage in some research themselves. We repeatedly hear of the synergistic relationship of education and research, and this exists in nursing education too. Today's nursing education programs will provide knowledge and patterns of behavior which will probably be used for several decades. For this reason, the best possible teaching knowledge and skills should be available, and we may have to do original research to find out what this knowledge and these skills should be in our changing professional world. Many of us would like to see hospitals offer their key nursing service personnel the opportunity and time to study and engage in research projects which might have direct bearing on the problems encountered in their home hospitals.

Clarity of statement of the problems to be studied is another area to be developed. Nurses who are working with researchers from other disciplines do not always express their ideas clearly and emphatically enough. They should be encouraged to remember (and here our medical colleagues can be helpful) that they are the experts in nursing. Some projects directed by non-nurse investigators have come up with some rather spurious and even ridiculous conclusions because the nurse on the research team was so awed by research language and methodology that she forgot about the nursing problem involved.

We still have to contend with the scoffers, particularly in related disciplines, who have the erroneous idea that we are trying to make researchers out of all the nurses in the country. They visualize the nurses running from the bedside, leaving patient care, and engaging instead in research. But do those teachers doing research in general education deplete the ranks or do they add to the effectiveness of all? Perhaps in a negative way we should be encouraged by Schopenhauer's classification of the four stages of progress of a new idea or movement: first, it meets ridicule; second, silence; third, violent opposition; and fourth, acceptance. Perhaps the idea of using reasearch to solve some of the nursing problems today is in the stage next to acceptance.

It is true that the idea of research has an appeal and an exciting allurement to many nurses. We, as a profession, need to educate doctors and others about nursing research, to bring an awareness to nurses of the problems it involves, and to urge nurses to understand the researcher. We need to convey the idea that all nurses (especially those engaged in giving care to patients) can be alert to nursing problems close at hand and can express their hunches so that they can be considered for proper study. One of the great by-products of research in nursing can be better and keener observations of patients by staff nurses, which will improve nursing assistance to physicians. Nurses with research preparation who are assigned to the care of patients involved in medical research can be markedly helpful to the investigator, for they will understand the reasons for meticulous adherence to medical orders, prescribed treatments, the collection of specimens or other data, and especially for recording accurately everything observed.

Summary

The goals of research in nursing are to improve patient care and to know (1) what the most effective nursing care consists of, (2) how efficiently and humanely to give this care, (3) how to teach this care in the shortest time possible, and (4) how to develop the full potential nurse power of all levels of nursing personnel. It is seeking a way to bring the professional nurse closer to the patient, whether she is giving the care or showing others how to do this.

If nursing care is to continue to improve, to provide the skills needed to assist the doctor with the care of the patient, and to make maximum use of its numbers of personnel, nurses too must engage in and assume responsibility for research. We believe that the public, the doctors, and the allied professional groups will gain by research in nursing. We believe that patients will benefit by more skilled care which will give more effective results, by more sympathy and warm understanding, by a listening ear, and by intelligent, simple answers to their questions on health and care. Doctors will benefit by increase in skilled assistance on a 24-hour basis which will relieve them of as much of the load of patient care as possible, by having the assistance of more alert observers and reporters of patient response and activity, and, most important, by seeing that their patients receive nursing care which adds more effectively to the patient's progress, comfort, and satisfaction. The hospital administration will benefit by a more effective and efficient nursing service for the lowest cost possible, satisfied patients, and satisfied medical personnel. Nurses will have more satisfaction with patient care (responsibilities which are geared to patient care, not agency or hospital maintenance), a greater opportunity to contribute to patient care, and recognition of the importance of their own skills on the health team.

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PRELIMINARY COMMUNICATION

SEVERE INFECTIOUS MONONUCLEOSIS TREATED WITH CHLOROQUINE PHOSPHATE

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Several of the antimalarial agents, including the 4-aminoquinolines, have been found effective in the clinical management of diseases other than the protozoan infections. Significant anti-inflammatory action of these agents has been reported in the treatment of diskoid and systemic lupus erythematosus, rheumatoid arthritis, and certain photodermatoses.[1] The purpose of this report is to present four cases of clinically severe forms of infectious mononucleosis which show a peculiar symptomatic response to the administration of chloroquine phosphate.

The mechanism of action of chloroquine (Aralen) phosphate, a 4-aminoquinoline, as both an antimalarial and an anti-inflammatory agent is poorly understood. The drug is rapidly and nearly completely absorbed from the gastrointestinal tract and is selectively bound in various body tissues. From 200 to 700 times the plasma concentration is found in liver, spleen, kidney, and lung. The skin and leukocytes also concentrate the drug or its degradation products heavily. Disappearance from the tissues requires several weeks. Degradation is mostly complete, and it is thought possible that the metabolic products may be the effective agents rather than the compound itself.[2] At sites of binding, the 4-aminoquinolines appear to have a strong interaction with nucleoproteins. Beyond this, little is known; however, Haydu, in 1953, suggested the possibility that the antimalarial agents act by inhibiting adenosine triphosphatase (ATP-ase).[3] This appears to be a tenable explanation of the mode of action of antimalarial agents in rheumatoid arthritis, in view of the evidence of increased tissue requirements for adenosine triphosphate in this disease, and may have a bearing on the chemotherapeutic effects in malaria as well. The antimalarial drugs have mild antipyretic effects of little usefulness and are inferior in this regard to salicylates.

Toxicity, except for transient symptoms such as headache, visual disturbances, mild gastrointestinal complaints, and pruritis, is not significant in the doses ordinarily used.

Report of Cases

CASE 1.—A 23-year-old railroad section-gang workman whose clinical course and response to treatment are shown in figure 1, was admitted to the Deaconess Hospital on Sept. 9, 1956, with marked malaise, chills, fever, nausea, and a progressive headache for eight days. He had been a patient at another hospital, six days prior to this admission, at which time he had not responded to antibiotic therapy.

On physical examination the patient appeared acutely ill but basically healthy. The oral temperature was 99.8 F (37.6 C), pulse rate 76 per minute and regular, and blood pressure 118/66 mm. Hg. Findings of ear, nose, and throat examination were negative, and the chest was normal to percussion and auscultation. The heart was not remarkable. Abdominal examination revealed a slightly tender liver edge palpable 2 fingerbreadths below the right costal margin, with the upper border of dulness in the fifth intercostal space in the right midclavicular line; the spleen tip was palpable and tender. Findings of genitourinary and rectal examinations, as well as of an examination of the extremities, were normal. Discrete, slightly tender lymph nodes were palpable in the posterior and anterior cervical regions and in both axillas and inguinal areas. Findings of neurological examination were normal. There was no icterus.

The initial hemoglobin level was 12.6 Gm.%; erythrocyte count 4,500,000 per cubic millimeter; white blood cell count 4,750 per cubic millimeter, with a differential count of 68% lymphocytes, 21% segmented neutrophils, and 11% band cells. Many of the lymphocytes were atypical forms. Urinalysis revealed a specific gravity of 1.036; an acid reaction; negative results of tests for albumin, reducing substances, acetone, and bile; and unremarkable microscopic findings. Erythrocyte sedimentation rate (Westergren) was 44 mm. per 15 minutes, 36 mm. per 45 minutes, and 111 mm. per 60 minutes. The total serum protein level was 6.6 Gm.%, with albumin 4.5 Gm.%, globulin 2.1 Gm.%, and albumin-globulin (AG) ratio 2:14. Agglutination titers for Brucella abortus and paratyphoid groups were not significant. Heterophil agglutination after absorption with guinea pig antigen was positive at 1:896

Read before the Annual Meeting of the Spokane Society of Internal Medicine, May 12, 1958 and after absorption with beef antigen was positive at 1:224. Blood, stool, and urine cultures failed to reveal pathogens. Result of examination for Leptospira was negative. Two days after the patient's admission the white blood cell count was 6,500 per cubic millimeter, 65% of which were lymphocytes, mostly abnormal forms and considered compatible with the diagnosis of infectious mononucleosis. Findings of a roentgenogram of the chest and an electrocardiogram were normal.

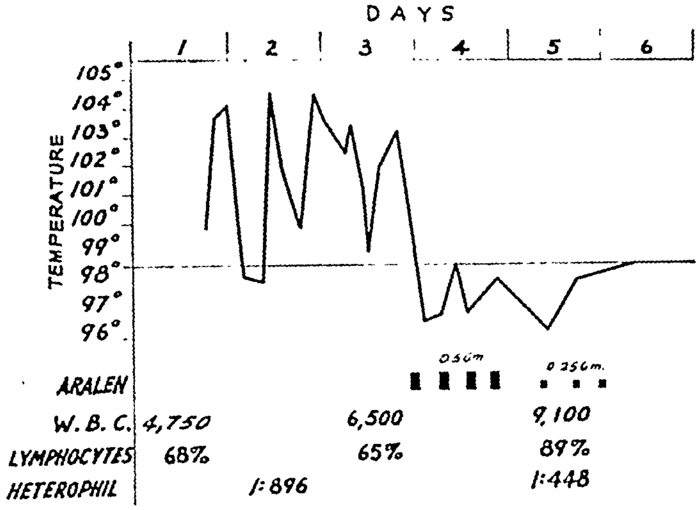

Fig. 1 (case 1).—Clinical course and response to chloroquine phosphate therapy of patient with infectious mononucleosis.

The patient continued to have abrupt chills, with temperatures rising to over 104 F (40 C) daily through the third hospital day. Malaise was marked during the febrile periods, but between these the patient was comfortable except for anorexia and mild headache. Fluid intake and output remained satisfactory. Initially no treatment but 15 grains (1 Gm.) of aspirin as required and 1½ grains (0.1 Gm.) of pentobarbital (Nembutal) at bedtime was given until 10:30 p. m. on Sept. 11, when chloroquine phosphate, 0.5 Gm., was administered. Administration of this dose of chloroquine was repeated at 6 a. m., and again at 12 noon and 6 p. m. on Sept. 12. The dosage was then reduced to 0.25 Gm. every eight hours for three doses, resulting in a total of 2.75 Gm. of chloroquine administered to the patient.

The patient's clinical improvement after receipt of the initial dose of chloroquine was striking. He reported a marked alleviation of all symptoms within six hours of the first dose and remained afebrile and asymptomatic through the day until his discharge on Sept. 14. On Sept. 13, physical examination revealed a slight though definite reduction in tenderness of liver and spleen, although no marked change in peripheral adenopathy was noted. Thirty-six hours after initiation of chloroquine therapy the white blood cell count was 9,100 per cubic millimeter, with a differential count of 89% lymphocytes, 1% monocytes, 4% segmented neutrophils, 5% band cells, and 1% eosinophils. The heterophil agglutination titer was 1:448. Follow-up reports from the patient's referring physician after one and two months, respectively, indicated an apparently complete recovery, without relapse. Unfortunately, a follow-up report on laboratory data could not be obtained.

Case 2.—A 26-year-old woman whose clinical course and response to treatment are show in figure 2, was admitted to the Sacred Heart Hospital, on April 26, 1957, with a history of malaise, fever, and enlargement of the cervical glands of about one week's duration. Her general health had otherwise been excellent. Physical examination revealed an oral temperature of 104 F (40 C); a large, tender anterior cervical lymph node on the right side and a small posterior cervical node on the left; and slight periorbital edema, with conjunctival injection. Findings of the rest of the examination were normal, except for moderate liver enlargement and tenderness to percussion, with the border 3 fingerbreadths below the right costal margin on deep inspiration. The initial erythrocyte count was 4,700,000 per cubic millimeter; white blood cell count was 2,150 per cubic millimeter, with a differential count of 30% neutrophils, 64% lymphocytes, and 2% eosinophils. The lymphocytes were mostly abnormal forms compatible with infectious mononucleosis. Urinalysis revealed 1+ albuminuria. The patient continued to show a variable fever response and was treated with tetracycline, 250 mg. four times daily, a compound containing acetophenetidin, acetylsalicylic acid, and caffein (Empirin Compound), and salicylates.

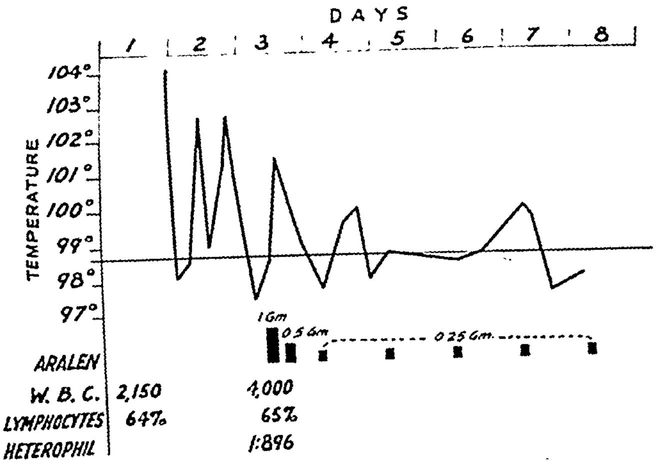

Fig. 2 (case 2).—Clinical course and response to chloroquine phosphate therapy of patient with infectious mononucleosis.

On the third hospital day chloroquine phosphate therapy was begun, with an initial dosage of 1 Gm. followed by 0.5 Gm. in six hours, and 0.25 Gm. daily thereafter during the remaining five days of hospitalization. The patient complained of slight nausea for a few hours after receipt of the initial dose of chloroquine but did not vomit. Within eight hours the patient's condition showed subjective clinical improvement and she felt well from the fourth hospital day until her discharge on the seventh day. On the third hospital day the white blood cell count had risen to 4,000 per cubic millimeter, with a differential count of 12% neutrophils, 21% stab cells, 65% lymphocytes most of which were atypical, and 1% basophils. The heterophil agglutination titer was 1:896. The patient was essentially afebrile from the fourth hospital day until her discharge, with a slight rise in temperature on the day prior to discharge.

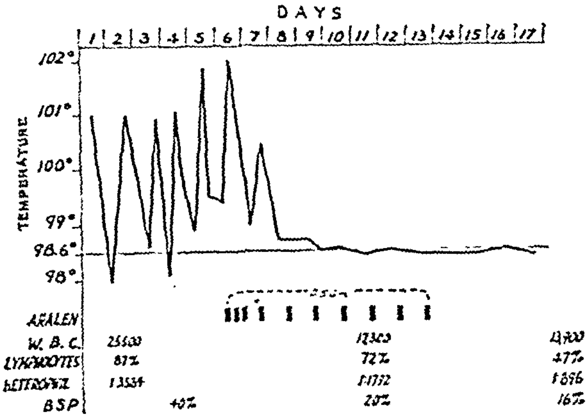

Fig. 3 (case 3).—Clinical course and response to chloroquine therapy of patient with infectious mononucleosis.

Case 3.—A 21-year-old soldier whose clinical course and response to treatment are show in figure 3, entered Fort Lawton Army Hospital on May 24, 1957, complaining of insidious onset of anorexia, malaise, sore throat, and fever. Examination revealed an oral temperature of 101 F (38.33 C), slight scleral icterus, generalized maculopapular eruption, enlarged red tonsils, large tender anterior and posterior cervical lymph glands, and hepatosplenomegaly. The initial white blood cell count was 25,000 per cubic millimeter, with a differential count of 13% neutrophils and 87% lymphocytes. Heterophil agglutination, unabsorbed, was positive in a dilution of 1:3,584. Other laboratory results included urine positive for bile, urine urobilinogen present in dilution at 1:48, serum sulfobromophthalein retention 40% in 45 minutes, serum bilirubin level 4.2 mg.%, cephalin flocculation 3+, and thymol turbidity 7 units.

Despite bed rest and symptomatic therapy the patient's condition did not improve, and daily remittent fever spikes to 101 and 102 F (38.33 and 38.89 C) were noted. On May 29, the sixth hospital day, chloroquine phosphate, 1.5 Gm., was administered in three divided doses, followed by 0.5 Gm. daily for the next seven days through June 5. Defervescence to normal promptly occurred, the patient continuing afebrile from June 1 for the rest of his hospital stay. Concomitantly, dramatic general symptomatic improvement and moderate euphoria were noted. On June 3, the sixth day of chloroquine therapy, findings of physical examination were normal except for slight splenomegaly. Laboratory examinations at this time revealed a white blood cell count of 17,300 per cubic millimeter, with 72% lymphocytes, heterophil agglutination positive in dilution of 1:1,792, sulfobromophthalein retention 20% in 45 minutes, serum bilirubin level 1.2 mg.%, urine negative for bile, and urine urobilinogen present at 1:20 dilution.

On discontinuance of chloroquine therapy the patient continued asymptomatic without discernible relapse. Laboratory studies done on June 10, however, revealed persisting abnormalities, including a white blood cell count of 13,900 per cubic millimeter, with 47% lymphocytes, heterophil agglutination positive in dilution of 1:896, and 16% sulfobromophthalein retention in 45 minutes.

Case 4.—A 16-year-old female student, whose clinical course and response to treatment are presented in figure 4, was first seen on Nov. 29, 1956, because of fever, sore throat, malaise, fatigue, and anorexia of two days' duration.

Physical examination revealed a somewhat obese girl, who appeared acutely ill. The oral temperature was 100.8 F (38.2 C), pulse rate 110 per minute, and blood pressure 120/82 mm. Hg. There was no icterus or skin rash. The ear, nose, and throat examination revealed markedly enlarged tonsils, with purulent exudate in the crypts. Large tender lymph nodes were palpable in the submaxillary and posterior cervical regions. The liver edge was not palpable; however, the tip of the spleen was felt just below the left costal margin on deep inspiration. The remaining findings of a complete physical examination were normal. The initial white blood cell count was 16,500 per cubic millimeter, with a differential count of 17% neutrophils, 49% lymphocytes, 5%

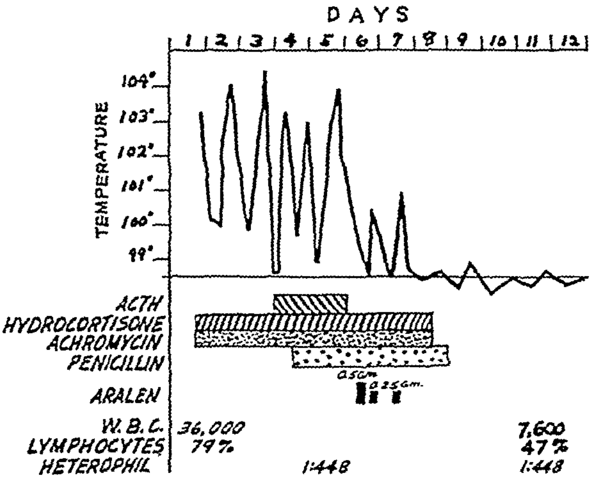

Fig. 4 (case 4).—Clinical course and response to chloroquine therapy of patient with infectious mononucleosis.

monocytes, 27% large (atypical) lymphocytes, and 2% eosinophils. The heterophil antibody titer was 1:448.

The diagnosis of infectious mononucleosis was made, and the patient was sent home to remain at complete bed rest. Therapy with tetracycline (Achromycin), 250 mg. every six hours, was started because of the severe pharyngeal reaction.

The next day, Nov. 30, the patient was definitely worse and was therefore admitted to Sacred Heart Hospital. A repeat examination at that time revealed no significant changes from the previous day, other than a temperature of 103.2 F (39.5 C) and a white blood cell count of 36,000 per millimeter. The differential count was 15% neutrophils; 79% lymphocytes, of which 15% were large and atypical; and 6% monocytes. The hemoglobin level was 13 Gm.%, and the erythrocyte count 4,300,000 per cubic millimeter. Urinalysis of a noncatheterized specimen revealed a pH of 5, specific gravity of 1.018, a trace of albumin, no sugar, and at microscopic examination 2 to 4 erythrocytes and 3 to 6 pus cells per microscopic field. A roentgenogram of the chest taken on Dec. 1 showed bilateral pleurisy and pneumonitis. A repeat determination of the heterophil antibody titer was 1:896 on Dec. 4, and after guinea pig absorption it was 1:448. Liver function studies revealed a sulfobromophthalein retention of 20% in 45 minutes, thymol turbidity of 2.5 units, and cephalin flocculation of 3+ in 48 hours. A throat culture was positive for alpha hemolytic streptococci which were most sensitive to penicillin and the tetracyclines.

The patient was treated with penicillin, 1,200,000 units twice daily; tetracycline, 250 mg. every six hours; hydrocortisone, 100 mg. intramuscularly daily; bed rest; and intravenously given fluids. Despite such treatment, her temperature continued to rise to 104 F (40 C) daily for the next five days. On Dec. 3, purified corticotropin (Acthar),-gel, 40 units, was given intramuscularly and the injection was repeated the next day; however, this also had no apparent effect on the course of the illness. The patient appeared extremely toxic and was having difficulty with respiration because of the marked tonsillitis and pharyngitis.

On Dec. 5, the patient was given 0.5 Gm. of chloroquine phosphate at 11 a. m. because of the response previously noted in another patient with infectious mononucleosis. She subsequently received 0.25 Gm. at 6 p. m. of the same day, and again at 7 a. m. the next day, Dec. 6. On the latter day her temperature rose to 100.8 F (38.2 C) and thereafter remained within normal limits. The patient's pharyngitis and tonsillitis promptly subsided, and her general improvement was striking. On Dec. 8 administration of all medicaments (penicillin, tetracycline, hydrocortisone, and chloroquine) was discontinued because of a mild maculopapular eruption on the chest and abdomen; however, the patient continued an uneventful recovery.

Laboratory studies performed on Dec. 10 revealed a white blood cell count of 7,600 per cubic millimeter, with a differential count of 43% neutrophils; 2% eosinophils; 47% lymphocytes, of which 21% were large atypical forms; and 8% monocytes. The heterophil antibody titer was 1:448 after guinea pig absorption. A subsequent differential count on Dec. 19 still revealed a relative lymphocytosis, and liver function studies done on Jan. 4 showed a cephalin flocculation of 4+ in 24 hours and no sulfobromophthalein retention in 45 minutes. At this time the patient had no complaints, and findings of a physical examination were normal. When seen again one month later, there was no evidence of relapse.

Comment

The rationale for the use of cloroquine phosphate in case 1 was the history of possible exposure to malaria and the wide temperature variation with relatively asymptomatic afebrile periods. It was thought that, despite negative blood smears, the patient may have had a reactivation of malaria associated with the splenic effects of infectious mononucleosis. However, in view of the responses observed in the patients in the succeeding cases, this explanation does not appear correct. There is no doubt that the subjective and objective improvement in these patients was dramatic and sustained. Furthermore, it must be emphasized that all were severely ill patients requiring hospitalization. In addition, a number of ambulant patients were treated. Although rapid symptomatic improvement occurred within one to two days of initiation of chloroquine therapy, and the lymphadenopathy appeared to decrease more rapidly than ordinarily would be expected, it is impossible to document these later cases effectively.

In none of the patients was the lymphocyte count or morphology affected, nor did the heterophil agglutination titer show an earlier than usual fall, except in the patient in case 4. In this instance, the drop in lymphocyte count was most likely due to ACTH and glucocorticoid therapy. In the patient in case 3 late evidence of hepatic dysfunction was noted, despite early immediate symptomatic response.

The patients in cases 1 and 2 received fairly large doses of salicylates prior to chloroquine, without significant antipyretic effect. The patient in case 4, with anginose manifestations, had shown no observable response to hydrocortisone and antibiotics used prior to the administration of chloroquine.

To attempt an explanation of this peculiar effect is not wise at this point, particularly when recalling that an agent of virtually unknown mode of action was used empirically in the treatment of a "disease" that is equally mystifying. If one accepts Goldthwait's[3] definition of infectious mononucleosis as a disease manifesting lymphoid hyperplasia, circulating abnormal lymphocytes, and heterophil antibodies which are absorbed by ox blood cells but not by guinea pig kidney, and if one considers as probable the concept of multiple etiologies, as proposed by Girard and Murray,[4] the presence or absence of the clinical response to chloroquine in given instances may prove to be of value in more narrowly defining the clinical syndrome. The clinical effect in these patients is as dramatic as that reported from the use of corticotropin[5] and, as in case 4, appeared to be superior thereto.

Whether the drug's effect is an antibiotic or chemotherapeutic one directed against an organism at an intracellular site remains to be studied. The failure to abort the antibody response or prevent secondary hepatic dysfunction suggests that a phenomenon of clinical suppression, analogous to that seen in malaria, is present, and that the slow disappearance of the tissue-bound forms of the drug may have produced a superficial clinical effect which outlasts the natural course of the acute phase of a self-limiting infection. The heavy selective concentration of chloroquine and its products in the very tissues which appear most affected by the disease, however, makes further clinical trial highly interesting, particularly with regard to the effects of treatment at earlier stages in the acute phase. The peculiar mild euphoria experienced by these patients and others treated with chloroquine is also of interest although not easily explained. It is hoped that, with further observations, of both positive clinical responses and treatment failures, a better understanding of infectious mononucleosis may eventually arise and additional light be shed on the mechanism of action of the 4-aminoquinolines. At present it can at least be said that symptomatic relief was highly gratifying in those patients who responded to chloroquine treatment.

Summary

Four patients with infectious mononucleosis, whose cases are described, showed a dramatic, and possibly specific, clinical response to treatment with chloroquine (Aralen) phosphate. Although the possible modes of action of chloroquine phosphate, as outlined here, are not entirely understood, further trial of the drug is warranted because of (1) the gratifying symptomatic relief patients obtained from its use and (2) the light that may be shed on the mechanism of action of the 4-aminoquinolines.

Paulsen Building (1).

Case 2 was reported with permission of A. M. Clark Jr., M.D., case 3 with permission of R. W. Burroughs, M.D., and case 4 with permission of A. B. Peterson, M.D. (deceased), Spokane, Wash.

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DIETARY PROBLEMS OF SUBMARINE LIFE.—The feeding problems inherent to living aboard a submarine have remained basically the same since a submarine was first developed which could remain at sea for more than a few days. The importance of these feeding problems, however, has increased steadily as submarine capabilities have improved. Immediately prior to the development of the nuclear-powered submarine, the limiting factor in the time a submarine could remain at sea was the amount of diesel fuel it could carry. Depending on its size and operating speeds, a submarine could remain at sea for periods up to 100 days. With the successful development of nuclear-powered reactors and oxygen-generating equipment, the United States was able to build submarines which can remain at sea for as long as two years. Food has thus become the time-limiting factor in submarine operations.—J. H. Schulte, M.C., U. S. Navy, Feeding Problems in the Submarine Service, *Journal of the American Dietetic Association*, April, 1960.

THE JOURNAL
OF THE AMERICAN MEDICAL ASSOCIATION

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ELECTRONIC DATA PROCESSING APPARATUS

DEVELOPMENTS during the past two years indicate that the electronic computer is rapidly achieving a place as a recognized tool of medicine. Although most of the applications so far have been exploratory, it is apparent from the results obtained that another important tool is rapidly developing to assist the physician and clinical investigator. The clinical application is described in this issue of THE JOURNAL by Schenthal and others, page 6. Electronic computers are basically of two types, the analog and the digital. The analog type of computer has long been familiar as the electrocardiograph and the electroencephalograph. The basic principle of an analog device is to measure one or more input variables and to transform them into proportional units of electricity. Thus, various aspects of the heartbeat are transformed into electrical current which is then visually presented by means of an ink graph. The analog computer can perform arithmetical manipulations on a number of inputs by means of organizing its circuitry into an electric analogy to the operations and presenting the answers in units of electronic energy which can be read by meters which transform either voltage or current variations into a visual medium.

A great deal of interesting work is being done to provide equipment which will automatically and continuously convert the results of an analog device into digital form such that the results can be transmitted directly to a digital computer for processing. The teaming together of the analog and the digital computer presents the most interesting opportunity for almost instantaneous and continuous analysis of physical phenomena.

The second type of computer, the electronic digital computer, is the newcomer to the medical world. Whereas the analog computer works with inputs of information which are sensed in many different ways and then converted internally into corresponding units of electricity, the electronic digital computer has its input in the form of representatives of discrete digits. The input digit to a digital computer can be any symbol which the computer has been designed to accept. Thus, practically all present-day computers accept both numerical and alphabetic input. Internally, the electronic digital computer transforms the input of information into various configurations of electronic pulses. These pulses are manipulated through the various circuits of the computer, and they can either be stored in the machine's memory or result in an output, also in digital form.

All electronic digital computers consist of four basic components. These components vary in capacity, speed, and electronic hardware but their functional relationship to one another and to the computing process remains constant. These components are the input-output units, the arithmetical unit, the control unit, and the memory system.

The input-output devices are the means by which either human beings or other machines communicate with an electronic computer. The most common medium of input-output information is the punch card. By this method information is punched into a card which is then fed into a card reader. The card reader is electronically connected with the computer and transforms the information which is in a representation of punched holes in the card into a representation of electronic pulses with the circuitry of the computer. In communicating answers, to a human being or another machine, the process is reversed and the computer transforms information which it carries within its circuitry in the form of pulses through the card punch into punched cards which then can be translated into a printed page for human consumption.

The arithmetical component in an electronic digital computer performs the simple functions of arithmetic in a manner similar to that of the desk calculator, except that the manipulations are done electronically rather than mechanically. The circuitry within the arithmetical component conducts the informational pulses through circuits which are pre-set for the information to be added to, subtracted from, multiplied by, divided by, or compared with another piece of information. The digital computer performs no arithmetical operation which cannot be performed by man, either in his head or with a pencil and paper. The advantage of the computer lies in the immense speed with which it can perform these operations and the high degree of accuracy that the computer can maintain when dealing with a long series of arithmetical manipulations or a large volume of information.

The control component of the computer consists of electronic circuits which monitor and coordinate all other components of a computer system. It is the function of the control unit to direct and coordinate the flow of information entering and leaving the system and the flow of information between the arithmetical component and the memory component. It also pre-sets the arithmetical circuitry to carry out the sequential steps of solution of a given problem.

The memory component of a computer system functions as a retainer of information. It can be in the form of an electronic core memory, a memory drum, or magnetic tapes. Each functions on basically the same principle. The electronic pulses which represent digital information are transformed into magnetic conditions. On a magnetic tape, for example, a series of electronic pulses which would represent a series of digits are fed into a reading head under which a magnetic tape similar to that used in the ordinary tape recorder is passing at high speed. The reading head transforms these pulses into magnetic spots on the tape as the tape passes under the head. When the computer wishes to read the tape, the process is reversed. As the section of the tape which contains the magnetic spots passes under the reading head, the spots are transformed into electronic pulses, which are fed back into the computer system. The advantages of the memory system of the computer are speed, accuracy, and compactness. A representative tape memory can store and recover from a single tape reel, 10 in. in diameter, over 5 million pieces of information. This information can be read by the computer at a rate of 15,000 pieces of information per second. The data going in and out of any tape unit are monitored by the system in many different ways, thereby maintaining a high degree of accuracy.

A digital computer needs two things to function in the solution of any problem. It needs a series of instructions as to how the problem is to be solved and the data which the computer is going to use in the solution of the problem. A person who uses the computer must go through certain steps in the preparation of his problem for the computer. He first must select a method of solution. This method of solution must be broken down into detailed sequential steps which the computer is capable of carrying out. This is the process of computer programming. The program is then put into a form which the computer can read. This is coding. In most cases this process involves punching the coded steps of a program onto punch cards. Next, the data to be used in the solution of the problem are put into a form which the computer understands. Again, this usually means putting the data into a punch card which can be fed into the input unit of the system.

The processing of a problem by a computer system is relatively simple. The coded program is fed into the system through the input unit and onto one of the memory systems of the machine. After this has been done the machine has within its memory all of the steps it must carry out to achieve a solution of the problem. The data for the problem are then made accessible to the input unit where the computer can call for the information as it needs it. The computer is then sent to read the first step of the program in its memory. From then on, the computer under its own control must carry out these steps it has within its memory sequentially.

The electronic digital computer offers to medicine the possibility of entering areas of inquiry which have not been possible in the past because of the time consideration due to the complexity of the method of solution or to the complexity and magnitude of the information involved. The computer in its true form is nothing more than an extension of the person's mind. However, it offers advantages of speed and capacity which enable the mind to explore problems which have been previously physically prohibitive. Unfortunately the computer has achieved a reputation as a statistical and mathematical machine. Although it does offer tremendous advantages in these areas the abilities of the computer as an information machine should not be overlooked. The computer has the ability to store great masses of heterogeneous information at high speed into physically compact form. It can also retrieve part or all of this information at tremendous speed. With this ability, the computer would appear to be an instrument for accumulating and storing complex medical records. Because of the high-speed manipulative skill of the computer and the high speed at which records can be interrogated it would appear that all medical information, experimental or clinical, could function by means of the computer both as data for research and as all or part of a retrievable historical medical record.

PREDOCTORAL COMPOSITION

The acceptance of the degree of Doctor of Medicine, granted by the governing authority of a medical school, is one of the most significant events in the professional life of a physician. Intimately entwined in the award of the degree is the implication that the recipient will hereafter be qualified to prepare a manuscript suitable for publication in a scientific periodical such as THE JOURNAL *of the American Medical Association*. This implication is valid and may be documented by a perusal of the records. Although graduation is an event concomitant with commencement, this does not necessarily grant licensure for the commencement of composition. On the other hand, good scientific composition usually is not born on graduation day. This may have had its beginning in precollege years or in a liberal arts discipline. If so, this is commendable.

There is need for greater interest and greater expenditure of efforts by the potential physician in description of experimental observations, written expression of thoughts, and formulation of conclusions. I am confident that much may be accomplished by counsel and encouragement. Counsel usually comes from professional preceptors, who probably are associated with the medical faculty responsible primarily for the teaching of a predoctoral candidate. If the medical student seeks assistance in composition, the teacher will be more than eager to foster this secondary goal in medical education. Encouragement of predoctoral composition also is one of the responsibilities of editors of medical journals. The door to The Journal has never been closed to medical students, but sympathetic encouragement has not been a characteristic of the past. Is encouragement justified?

A number of notable examples of achievement by medical students during the past four centuries has been compiled by Gibson in "Young Endeavor."[1] Paul Ehrlich became interested in the staining reaction of tissues during his undergraduate days at the University of Strasbourg. Ivan Pavlov was appointed the director of scientific investigation in the most famous clinic of Internal Diseases in Russia before he was awarded his Doctorate of Medicine. Edward Jenner, at the age of 19, sensed the significance that an attack of cowpox had in protecting a person against smallpox. Sir James Paget, as a first-year medical student, identified the calcified spicules of Trichina infestation. Finally, Daniel Carrion, who gave his life in order to test the hypothesis that verruga peruana could be transmitted in the blood, died before he finished his medical course, from a case of this malady near Oroya in central Peru. Gibson has enumerated more than 60 predoctoral contributions from famous physicians in the past; he has wisely omitted any reference to contributions of living physicians.

It is the current editorial policy of The Journal to foster communications from medical students. This is not condescension. No favoritism will be shown. The blindfold test will be employed in reverse—the editor will wear the blindfold, not the investigator in reviewing the professional status of the student. The predoctoral communication will stand in competition with postdoctoral efforts. Two gains may be realized with the passage of time. First, if competition becomes sufficiently acute, the postdoctoral writer may expend greater effort in planning the experiment, gathering data, and telling the story. Second, the predoctoral writer may continue after graduation to pursue the third phase with great skill. The contemporary medical student already is exposed to proper indoctrination in the first and second phase. If the third phase is exploited in medical school, the encouragement offered by the school's editorial division may contribute to proficiency in composition in the professional years.

Communications to The Journal from medical students are welcome. This statement applies to original communications, preliminary communications, contributions in clinical science, correspondence, or medical satire. If the physician of tomorrow is expected to contribute to the scientific literature, it is not too early to prepare. The communication from Townsend and Luckey in this issue was written by a medical student, assisted by his preceptor in pharmacology. It was the result of a project pursued on elective time. Other communications from medical students will be published whenever the standards for acceptance of manuscripts are satisfied.

J. H. T.

RESOLUTION DEADLINE

Deadline for resolutions to be submitted to A. M. A.'s House of Delegates for its 1960 Annual Meeting is 12 noon, June 12. Resolutions should be mailed to reach Dr. F. J. L. Blasingame, executive Vice-president, American Medical Association, 535 N. Dearborn, Chicago 10, by June 1.

THE HOSPITAL—MANY HANDS AND MANY SKILLS

This succinct title is also the theme of the 1960 National Hospital Week, to be observed May 8 through May 14th. For this particular week, the spotlight is turned on the growing complexity of hospital services and on the personnel who provide these services. Hospitals throughout the nation are planning special programs in observance of this week. They are seeking the support and cooperation of their medical staff physicians, for physicians can do much to create better public understanding of hospitals.

Today the hospital plays an increasingly important role not only in medical research, in formal medical education, and, through medical staff activities, in the continuing education of the physician but also in the practice of medicine. Each year more and more patients are cared for in hospitals, under their physicians' direction, because of the trained teamwork centered in the hospital to aid in diagnosis and therapy and to speed recovery. Good medicine and good hospitals are mutually inclusive and mutually dependent.

Hospitals face a perpetual dilemma. They must meet demands for efficiency and economy yet keep pace with medical progress; they must streamline services and use good business practices, but they must meet human needs and gear their services individually to the orders written by the physician. Those orders, calling into action a complex of trained teams behind the scenes and at the patient's side, determine patient care and patient costs. Expenditures for the more routine services such as food service, housekeeping, maintenance, and laundry have been held below the inflationary curve by use of more efficient methods. The greatest increases in hospital costs, rising above the inflationary curve, have occurred in nursing and in the professional service departments such as laboratory, operating room, and pharmacy, reflecting the expansion in the number, variety, and volume of services.

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[1] Gibson, W. C.: Young Endeavor, Springfield, Ill., Charles C Thomas, Publisher, 1958.

The "many hands and many skills" which perform these services are a far greater factor in hospital costs than is the most expensive equipment. In the short-term voluntary hospitals, leaders in the development of comprehensive services, the ratio of personnel to patients now averages 2.2, as compared with 1.5 only 12 years ago. Payroll costs per patient stay in these hospitals have nearly tripled, whereas nonpayroll costs have not quite doubled, during this same period.

Significant reduction in hospital costs is not possible without reduction in the number and variety of services provided to the patient. Physicians of course want to avoid overuse or unnecessary use of hospital services but never at the expense of good patient care. They should be alert to the threat of externally imposed controls which would establish cost ceilings for hospitals, without respect to human needs, medical judgment, and medical progress. This threat to hospitals and physicians can be averted only if both work together to create understanding of the nature of hospital costs.

CHANGE OF FOLIO

Approximately 18 months ago a stipulation of the U. S. Postoffice Department required the front-to-back numbering of pages (folio) in medical periodicals that carried a substantial number of full pages of advertising. I recall the confusion that this innovation brought to my mind when I discovered a light and a dark series of numbers on the pages of The Journal. It was not until later that I learned of my failure to read a previous issue (*J. A. M. A.* 169:47 [Jan. 3] 1959) which described the necessary action taken by my predecessor, once removed. Austin Smith had no choice in the decision. It was necessary to include bold face and light face numbers to satisfy the postal regulations.

It has been determined now after considerable deliberation that it is permissible to place the light folio at the bottom of each page. The bold face pagination remains in the characteristic position. This is another example of the firm desire to improve the format of The Journal and to enhance acceptance of a widely read scientific periodical.

J. H. T.

CANCER CELLS IN THE BLOOD STREAM

Six years ago Cole, Packard, and Southwick[1] reported finding cancer cells in fluid perfused through the artery and collected from the vein of a cancerous segment of colon removed at operation. Other investigators have reported finding cancer cells in the circulating blood. In a recent study[2] of 328 patients with malignant disease, cancer cells were found in the peripheral blood in 23% of the "curable" cases and in 33% of the "incurable" cases, in some before, in some during, and in some after operation.

These investigators saw showers of cancer cells in blood specimens in some cases incident to manipulation of the tumor by such means as pelvic physical examination, dilation and curettage, preparation of the skin prior to operation for cancer of the breast, application of a pedicle clamp, and dissection about the tumor.

Moore, Sandberg, and Watne[3] recently reported a study of 179 patients with advanced cancer in whom one-half of the peripheral blood samples contained tumor cells. They, too, emphasize that tumor cells may be spread by the physician and surgeon during the examination of patients, diagnostic procedures, and operative manipulations.

The full significance of the presence of cancer cells in the blood is not known. There is a time when cancer cells do not appear in the blood stream, a time when they do appear and are killed by the patient's natural defenses, and a time when the patient's resistance is low and these cells grow, metastasize, and kill the patient. Engell[4] in his five-to-nine-year follow-up study concluded that, in most patients surviving that long, tumor cells disseminated before and during operation must have perished in the blood stream. Moore, Sandberg, and Watne believe that probably 99.9% of all tumor cells released into the blood stream fail to survive and establish metastases. Undoubtedly many of these circulating cancer cells are destroyed by the natural defenses of the human body. Undoubtedly some of them metastasize.

These carefully conducted studies should interest all physicians. However, they are of immediate importance to practicing physicians, whom they advise: Do nothing by way of manipulation to a patient with malignant disease which might cause cancer cells to enter the blood stream.

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1. Cole, W. H.; Packard, D.; and Southwick, H. W.: Carcinoma of Colon with Special Reference to Prevention of Recurrence, J. A. M. A. **155**:1549-1553 (Aug. 28) 1954.
2. Long, L.; Roberts, S.; McGrath, R.; McGrew, E.; and Cole, W. H.: Cancer Cells in Blood Stream, A. M. A. Arch. Surg. **80**:639-645 (April) 1960.
3. Moore, G. E.; Sandberg, A. A.; and Watne, A. L.: Spread of Cancer Cells and Its Relationship to Chemotherapy, J. A. M. A. **172**:1729-1733 (April 16) 1960.
4. Engell, H. C.: Cancer Cells in Blood: 5 to 9 Year Follow up Study, Ann. Surg. **149**:457-461 (April) 1959.

MEDICAL NEWS

CALIFORNIA

Dr. Murphy Named University Chancellor.—Dr. Franklin D. Murphy, presently chancellor of the University of Kansas School of Medicine, will become chancellor of the University of California at Los Angeles on July 1. Appointment of Dr. Murphy was approved March 16 by the University of California Board of Regents. He will replace Chancellor Vern O. Knudsen, who reaches the administrative retirement age of 67 this year. Dr. Murphy received his medical degree in 1941 from the University of Pennsylvania. In 1948 he became dean of the UK School of Medicine and in 1951 became chancellor. Dr. Murphy is chairman of the executive committee of the Commission on Higher Education in the American Republics, a group of presidents of American and Latin-American universities. He is also chairman of the U. S. Advisory Commission on Educational Exchange of the Department of State, which governs the Fulbright program. In 1949, the U. S. Junior Chamber of Commerce cited Dr. Murphy as one of its 10 "outstanding young men."

Civil Defense Test Exercise.—The threat of imminent nuclear attack and an order for the general evacuation of civilians from a metropolitan area will set the stage for Operation Defiance, a civil defense test exercise to be held during Medical Civil Disaster Week, June 13-18, in the Oakland area under the sponsorship of the Alameda–Contra Costa County Medical Association, the California Disaster Office, the Oakland Department of Civil Disaster, and the 352nd Army Reserve General Hospital. Five major Oakland hospitals will evacuate all transportable patients to a peripheral safe area in phase one. Phase two will begin after 2½ hours of the first phase with an alert signal warning of attack within a half hour. Further evacuation from the hospitals will immediately cease and rapid movement of hospital patients to survival wards will occur. Phase two will end with the take-cover signal. Monitored and evaluated will be demonstrations of evacuation of patients, transportation, communication, staff reconstitution in a peripheral area, survival ward facilities and placement, the importance of law enforcement facilities in civil disaster, and command post operations.

FLORIDA

Resolution on Ambulance Violations.—The Hillsborough County Medical Association of Tampa passed a resolution concerning traffic and other violations of ambulances. The resolution reads, in part, as follows:

> Be It Resolved, that the Hillsborough County Medical Association go on record as approving the following:
> 1. All ambulance drivers be required to hold Red Cross First Aid certificates.
> 2. All ambulance drivers observe the traffic speed laws and cease the use of the siren except in extreme emergencies such as poisoning, gross hemorrhage or on specific instructions of the physician.
> 3. In case of the necessity of traffic violation, the ambulance drivers be required to file a certificate with the Police Department giving the name of the patient and diagnosis.
> 4. That some system of rotation be established to prevent several ambulances from rushing to the scene of an accident.
> 5. That in no case should an ambulance speed or use the siren on taking patients from the hospitals to their homes.

Center for Rehabilitation.—A rehabilitation center for patients with paralysis agitans will be constructed in Miami this summer. Ground-breaking ceremonies for the new center, to be built close to Miami's Metropolitan Medical Center, are scheduled for May 1. The center will be built and supported by the Florida chapter of the National Parkinson Foundation and will be operated under the supervision of the division of gerontology of the University of Miami School of Medicine. Dr. Samuel Gertman, associate professor of geriatrics at the medical school, is chairman of the medical advisory board. Focus will be on rehabilitation of the entire family of the patient. While physical disabilities will be treated, the goal will be a total rehabilitation. The Florida chapter will also provide three fellowships for basic and clinical studies in neurosurgery, neurology, and geriatrics in connection with this program. The work of the fellowship students in Miami will be coordinated with a program of basic research at the University of Chicago, supported by the National Parkinson Foundation.

ILLINOIS

Alumni Meeting in Chicago.—The Medical Alumni Association of the University of Illinois has scheduled its annual Medical Seminar for Monday, May 23, the day preceding the Illinois State Medical Society meeting. The annual banquet will be held at the Illini Union, 715 S. Wood St., following

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Physicians are invited to send to this department items of news of general interest, for example, those relating to society activities, new hospitals, education, and public health. Programs should be received at least three weeks before the date of meeting.

the day's program of seminars, lectures, and clinics. Officers for 1960-1961 will be elected following the banquet. Guest speaker will be Mr. Sydney J. Harris, *Chicago Daily News* columnist. Alumni and their guests are invited. For information, write Dr. Louis R. Limarzi, Associate Professor of Medicine, Room 216, University of Illinois Research and Educational Hospitals, 840 S. Wood St., Chicago 12.

Chicago

Annual Lecture.—The 10th Arthur William Stillians Lecture of the Metropolitan Dermatological Society of Chicago will be given at the annual meeting May 11 by Mr. William J. McAuliffe Jr., Law Division, American Medical Association, entitled "Doctor—You Can Solve the Malpractice Problem."

MARYLAND

Reregistration of Physicians.—The State of Maryland has reregistration of physicians triennially. This law becomes effective June 1. All physicians who possess a license to practice medicine and surgery in Maryland who have not received a registration application from the Board of Medical Examiners of Maryland by Sept. 1, 1960, should notify the office of the board immediately. This also includes physicians living out of state who possess a Maryland license to practice medicine and surgery and who wish to keep their Maryland licenses active.

MICHIGAN

Increase in Rabies.—The Michigan Department of Health announced that an increase in rabies among both domestic and wild animals occurred in the first quarter of the year, with 14 of 18 cases reported occurring in March. The public health veterinarian in the acute communicable disease section said the 18 cases in the first three months were 11 more than were reported in a corresponding period last year. Counties in which cases were reported are Allegan, two cats; Alpena, a skunk; Clinton, a skunk; Genesee, two dogs; Isabella, three skunks and a dog; Kalamazoo, a cat and dog; Manistee, a dog; Mecosta, a skunk and dog; Missaukee, a dog; Saginaw, a dog; and Van Buren, a skunk. The health department recommends the following preventive measures: (1) rabies vaccination of dogs and cats; (2) increased control over stray dogs and cats in communities; (3) keeping pets from running at large; and (4) leaving wild animals, particularly skunks, alone.

MISSISSIPPI

Annual Meeting in Jackson.—The 92nd annual session of the Mississippi State Medical Association will be held in Jackson, May 10-12, under the presidency of Dr. Stanley A. Hill, Corinth. Special scientific and social groups will meet May 9. Dr. E. Vincent Askey, Los Angeles, President-Elect, American Medical Association will be a participant, and other essayists will include the following:

Drs. Robert N. Buchanan Jr., Nashville, Tenn.; Guy A. Caldwell, New Orleans; Robert J. O. Coffey, Washington, D. C.; Charles W. Daeschener Jr., Galveston, Texas; Theodore K. Dampeer Jr., New Orleans; Daniel F. Fisher, Memphis, Tenn.; George M. Haik, New Orleans; Lawrence L. Hester Jr., Charleston, S. C.; and Arthur E. McElfresh, Philadelphia.

Scientific section meetings will be held in medicine, obstetrics and gynecology, pediatrics, preventive medicine, surgery, and eye, ear, nose, and throat. The annual association banquet will be held May 11, 7:30 p. m. A ladies' program is arranged. For information, write Mr. Rowland B. Kennedy, P. O. Box 4606, Fondren Station, Jackson, Miss., Executive Secretary.

NEW JERSEY

State Meeting in Atlantic City.—The Medical Society of New Jersey will hold its 194th annual meeting May 14-18 at Haddon Hall, Atlantic City, under the presidency of Dr. F. Clyde Bowers, Mendham. Nineteen scientific section meetings are scheduled and will include the following discussions and symposiums:

Heart Sounds and Murmurs.
The Medical-Legal Aspects of Cardio-Pulmonary Diseases.
Current Problems in Virus Diseases.
Constipation.
Geriatrics.
Indications and Contraindications for Tonsillectomy and Adenoidectomy.
Revascularization of the Lower Extremity with Arterial Insufficiency.

A program of medical motion pictures and exhibits are planned, and special lectures are scheduled. A dinner-dance will be held the evening of May 17. For information, write Mr. Richard I. Nevin, P. O. Box 904, Trenton 5, N. J., Executive Officer.

NEW MEXICO

Annual State Meeting.—The 78th annual meeting of the New Mexico Medical Society will be held May 8-14 at the Western Skies Hotel, Albuquerque. At the banquet for officers, delegates, and speakers the evening of May 10, Dr. Rufus B. Robins, Camden, Ark., member of the Board of Trustees, American Medical Association, will present "The New Look in Medical Practice." Dr. Lewis M. Overton, Albequerque, president of the state society, will give the presidential address the morning of May 11. The program includes the following panel discussions and moderators:

Special Senses, Dr. Arthur J. Fischer, Las Cruces.
Rehabilitation, Dr. Lewis M. Overton, Albuquerque.
Cancer of the Breast, Dr. Martin B. Goodwin, Clovis.
Skin Problems, Dr. John J. Corcoran, Albuquerque.
The Public Health Team, John Mason, D.V.M., New Mexico Department of Public Health.

Crippling Diseases of the Chest, Dr. Burgess L. Gordon, Albuquerque.
Skin Problems, Dr. Corcoran.

Two symposiums are planned: "The Improvement of Perinatal Morbidity and Mortality" and "Infectious Disease Control." Exhibits are planned and a ladies' program is arranged. For information, write Mr. Ralph R. Marshall, 220 First National Bank, Albuquerque, N. M., Executive Secretary.

NEW YORK

Annual Lilienthal Lecture.—At the 20th annual dinner meeting of the New York State chapter of the American College of Chest Physicians, Dr. Arthur Q. Penta, Schenectady, will present the 10th annual Howard Lilienthal Lecture, "The Role of Oral Infections in the Etiology of Pulmonary Suppuration." The meeting will be held May 10. Five additional papers are scheduled for the scientific program, to be held that morning. For information, write Dr. Harry Golembe, Box 310, Liberty, N. Y., Secretary-Treasurer.

Personal.—Dr. Willard J. Davies, of Rockville Centre, was appointed an expert consultant on dust diseases to the New York State Workmen's Compensation Board Feb. 10.——J. Garth Johnson, Ph.D., chairman, department of community health, Albany Medical College, retired as editor of the Association of Teachers of Preventive Medicine *Newsletter*. Dr. Johnson served as editor of the publication for seven years, 1953 through 1959. His successor is Dr. Duncan W. Clark of the State University of New York College of Medicine, Brooklyn. The newsletter is distributed to teachers of preventive medicine in the nation's 82 medical schools.

State Convention in New York City.—The 154th annual convention of the Medical Society of the State of New York will be held May 7-13 at the Statler Hilton Hotel, New York City. Symposiums and panel discussions to be presented at the general sessions are as follows:

Replacement of Organs and Tissues.
Medicine in the Space Age.
The Control of Cancer.
Clinical Potentialities of Hypothermia.
Advances in Cardiovascular Technics.

Dr. Carl R. Ackerman, New York City, of the United Medical Service, will present "Medicine and Blue Shield Meet the Challenge" as the A. Walter Suiter Lecture the afternoon of May 11. Section and discussion meetings will be held May 10 through May 13. Scientific and technical exhibits and a program of motion pictures are planned. A ladies' program is arranged. A dinner-dance will be held at the Hotel Pierre May 9, 7 p. m. For information, write Dr. Herbert T. Wagner Jr., 750 3rd Ave., New York 17, Executive Director.

Emergency Hospital Teams.—Since 1957 New York State has trained 110 community teams of physicians, nurses, hospital personnel, and medical aides to turn a school building into a surgical Improvised Emergency Hospital after an enemy attack. Thirty teams are scheduled to be trained during the basic part of a State Mobile Hospital Outfit. Two such training outfits are touring the state by trailer truck for use in this program and are loaned to the local civil defense organization conducting the training. Specialists from the New York State Department of Health assist with the training exercise which is divided into two sessions. At the first session boxes containing hospital supplies are unpacked and the hospital is set up. At the second session tagged litter-cots are used as simulated casualties, and treatment is simulated in the various hospital sections, so that members of the team have an opportunity to learn how to use the supplies and equipment furnished and how to obtain additional supplies. New York State has stockpiled 200 Mobile Hospital Outfits capable of treating 200 surgical patients for 10 days and capable of being expanded to treat 400-500 patients by means of stacked litter-cots, additional personnel, and additional expendable supplies.

NORTH CAROLINA

State Session in Raleigh.—The Medical Society of the State of North Carolina will hold its 106th annual meeting May 7-11 in Raleigh, with the House of Delegates meeting May 9. On May 10, United States Senator Sam J. Ervin Jr., Morgantown, will give an address, after which an address from the Student Scientific Section will be followed by the annual address of the president by Dr. John C. Reece, Morgantown. Papers to be presented by out-of-state speakers are as follows:

The Meaning of Curative and Palliative Radiation, Dr. Walter T. Murphy, Buffalo, N. Y.
Socio-Economic Aspects of Medical Practice and Medical Society Affairs, Dr. Leonard W. Larson, Bismarck, N. D.
Life Aboard a Nuclear-Powered Submarine, Lt. Commander Richard T. Arnest, Norfolk, Va.

Specialty group meetings, luncheons, and a postgraduate and audio-visual program are planned. A concurrent general session with the North Carolina State Board of Health is planned for May 11. For information, write Mr. James T. Barnes, 203 Capital Club Building, Raleigh, N. C., Executive Director.

OHIO

Dr. Doan to Retire as Dean.—Dr. Charles A. Doan, dean of the Ohio State University College of Medicine and director of the Health Center, will retire from these assignments by July 1, 1961. Dr. Doan, who also holds the additional titles of professor of medicine and director of medical research, has been on the College of Medicine faculty since 1930.

PENNSYLVANIA

Philadelphia

Lecture in Medical History.—The second Victor Robinson Lecture in the History of Medicine will be given at the Temple University School of Medicine, in conjunction with the presentation of portrait of Dr. Victor Robinson, with remarks by Dean Robert M. Bucher and Dr. Fred B. Rogers. The lecture, "The Role of History in Medical Education," by Richard H. Shryock, Ph.D., librarian, American Philosophical Society, and professor of history of medicine, Johns Hopkins University, Baltimore, will be given Wednesday, May 11, 4 p. m., *at the Medical School Auditorium.*

RHODE ISLAND

Annual Meeting in Providence.—The Rhode Island Medical Society will hold its annual meeting May 10-11 in Providence. Dr. Maxell Finland, Boston, will present "Antibacterial Agents: Uses and Abuses in Treatment and Prophylaxis" as the Chapin Oration. A panel on back pain will be moderated by Dr. Kenneth G. Burton, Providence, the morning of May 11. Papers to be presented by out-of-state speakers are as follows:

Direct Visual Approach to Acquired Valvular Heart Disease in Adults, Dr. J. Gordon Scannell, Boston.
Basic Requisites for an Adequate Compensation System, Dr. Alexander P. Aitken, Boston.
A New Approach to Treatment of Cardiac and Hepatic Edema by Steroids, Dr. Harry Gold, New York City.
Pulmonary Microcirculation, Dr. John W. Irwin, Boston.

Dr. Dean F. Smiley, Evanston, Ill., executive director, Educational Council for Foreign Medical Graduates, will present "Foreign Medical Graduates Service as Interns or Residents in U. S. Hospitals." Dr. Alfred L. Potter, Providence, will present the presidential address at the close of the scientific session. A dinner meeting is planned for 8:30 p. m., May 11. For information, write Dr. Arthur E. Hardy, 2 Post Rd., Warwick 5, R. I., Secretary.

SOUTH DAKOTA

State Medical Meeting in Aberdeen.—The 79th annual meeting of the South Dakota Medical Association will be held May 14-17 at the Alonzo Ward Hotel, Aberdeen, and will include the 50th anniversary of the Women's Auxiliary of the association. The program lists the following speakers:

Drs. Albert H. Andrews, Chicago; William T. Gibb, Washington, D. C.; Kenneth C. Johnston, Chicago; Kenneth Barrows, Des Moines; Kermit E. Krantz, Little Rock, Ark.; John E. Harris, Minneapolis; Joseph Jorgens, Minneapolis; John M. Berkman, Rochester, Minn.; H. Angus Bowes, Aberdeen; James E. Gilbert, Aberdeen; Claude R. Hitchcock, Minneapolis; Lyle V. Kragh, Minneapolis; John K. Grotting, Minneapolis.

Two forums are planned, and a panel discussion, "Respiratory Disease," will be held the afternoon of May 16 with Dr. Paul G. Bunker, Aberdeen, as chairman. The banquet and dinner dance will be held 7 p. m., May 16. A symposium on preceptorship the afternoon of May 17 will conclude the scientific session. President of the society is Dr. R. A. Buchanan, Huron. For information, write Mr. J. C. Foster, First National Bank Building, Sioux Falls, S. D., Executive Secretary.

TEXAS

Establish Hospital Lectureship.—The first annual Methodist Hospital Lectureship in Medicine sponsored by the hospital's department of internal medicine will be held in Lubbock at the auditorium of the Tom S. Lubbock High School, May 7. Lecturers will be Drs. William Dameshek, Boston, William H. Crosby, Washington, D. C., and Joseph M. Hill, Dallas. Dr. Hill will present three papers and Drs. Dameshek and Crosby, four each. The program is approved for eight hours category II credit by the American Academy of General Practice. For information, write Dr. Patrick H. Pappas, 3621 21st St., Lubbock, Texas.

VIRGINIA

General Practice Meeting.—The 10th annual scientific assembly of the Virginia Academy of General Practice will be held at the Cavalier Hotel, May 12-15. Papers to be presented by out-of-state speakers are as follows:

Acute Respiratory Diseases, Dr. Count D. Gibson Jr., Boston.
The Differential Diagnosis of Functional and Organic Diseases, Dr. Perry S. MacNeal, Philadelphia.
Cardiacs Can Work, Cardiacs Should Work, Dr. David Gelfand, Philadelphia.
Use of Hypnosis in General Practice, Dr. Jacob H. Conn, Baltimore.
Management of Acute Ocular Injuries, Dr. Ronald A. Cox, Washington, D. C.
Basic Principles of Electroencephalography and the Clinical Value of the EEG, Dr. James P. Murphy, Washington, D. C.
Differential Diagnostics in Childhood Anemias, Dr. Doris A. Howell, Durham, N. C.
A Workable Program for Senile Mental Changes, Dr. Arthur H. Dube, Syracuse, N. Y.
Manifestations of Pregnancy, Dr. Leslie V. Dill, Washington, D. C.

A program of entertainment includes a golf tournament May 12. A ladies' program is arranged.

GENERAL

Plan Neutral Medical Group for Wartime.—Pope John XXIII, gave support March 31 to a group that seeks to enlist the world's doctors in a non-national medical service during wartime. The Pope granted a special audience to a delegation of the International Committee for Medical Neutrality in Wartime headed by French Minister of Veterans' Affairs Raymond Triboulet. The committee's president, Charles Richet, told the Pope that his group hopes to set up a neutral medical organization on a world scale to offer aid to warring nations. He said it will function in connection with the International Red Cross.

Radiologists Receive Gold Medals.—Drs. Lawrence Reynolds, Detroit, and L. Henry Garland, San Francisco, were awarded gold medals for "outstanding contributions to the college . . . and the profession for which it stands," by the American College of Radiology. Presentation took place in New Orleans during the annual convocation Feb. 5. In other highlights of the meeting, Dr. Robert C. Pendergrass, Americus, Ga., was elected vice-president; and Drs. Stanley M. Wyman, Boston, D. Alan Sampson, Ardmore, Pa., and Wendell G. Scott, St. Louis, were elected to four year terms on the board of chancellors. The 1961 meeting of the college will be held in Chicago, Feb. 8-11.

Annual Meeting of Neurological Surgeons.—The annual meeting of the Congress of Neurological Surgeons will be held at the Palmer House, Chicago, Oct. 26-30. The honored guest will be Dr. Paul C. Bucy, professor of neurological surgery, Northwestern University Medical School, Chicago. The meeting will be oriented toward dealing with problems of the spinal cord and nerve roots. On Wednesday afternoon, Oct. 26, a half-day postgraduate course on neuro-otology will be conducted by Dr. John R. Lindsay, Holden, Mass. For information, write Dr. Richard L. DeSaussure Jr., Suite 101 B-20 South Dudley St., Memphis, Tenn., Secretary-Treasurer.

Meeting of Oto-Ophthalmological Group.—The Pacific Coast Oto-Ophthalmological Society is holding its annual meeting at the Hotel St. Francis, San Francisco, May 22-26. The following invited guest speakers will participate in the program: Dr. Edward S. Perkins, London, England; Dr. Adrian M. Ostfeld, Chicago; Dr. Edwin J. Wylie, San Francisco; Dr. Bruce N. Kvernland, Portland, Ore.; Dr. Jerome A. Hilger, St. Paul, Minn.; Merle Lawrence, Ph.D., Ann Arbor, Mich.; Dr. John R. Lindsay, Chicago; and Dr. Jack V. D. Hough, Oklahoma City. Room reservations for the meeting may be obtained by writing Mrs. Lorraine Berry, Housing Bureau, Room 300, 61 Grove St., San Francisco.

Request for Medical Journals.—The University of Hue, in the Republic of Vietnam, 50 miles south of the 17th parallel which divides free Vietnam from its Communist counterpart to the north, was established in 1957. The university intends to open a medical school in the near future. The organization American Friends of Vietnam is assisting in furnishing books and other educational materials to Vietnam universities. With the opening of the new medical school at Hue, it is planned to solicit medical textbooks, journals, and similar publications. Books and journals should be sent to the American Friends of Vietnam, Inc., Room 204, 4 W. 40th St., New York 18. Each gift will be acknowledged, catalogued, and prepared for shipment abroad.

Research Fellowships.—The United States Public Health Service announced the availability of fellowships for research under three categories. Candidates for the predoctoral fellowships must have a bachelor's degree or equivalent training. Candidates for postdoctoral fellowships and those for special research fellowships must have a doctor's degree or equivalent training. Stipends in the three groups range from $18,000 to $55,000 a year, and additional allowances are available for dependents and other expenses under the three fellowships. Applications may be made at any time. Information and applications may be obtained from the Research Fellowships Review Branch, Division of Research Grants, National Institutes of Health, Bethesda 14, Md.

Medical Women Meeting in Puerto Rico.—The Pan American Medical Women's Alliance will hold its 7th congress in San Juan, Puerto Rico, June 3-8, according to the president, Dr. Sarah H. D. Rosekrans, 504 Hewett St., Neillsville, Wis. The scientific program subjects include pulmonary disease, obstetric problems, special types of practice, pediatric problems, and miscellaneous papers. All papers will be presented in Spanish and English. The Pan American Medical Women's Alliance, organized in Mexico City in 1948, meets biennially, alternating between Spanish- and English-speaking countries. The president, president-elect, and vice-president are chosen with alternate representation. The purpose of the alliance is "to bring the medical women of North, South and Central America, and the Caribbean area into an association with each other for mutual improvement." For information regarding the congress, write Dr. Rosekrans at the above address.

Society News.—On March 19 the following were elected officers of the **Central Neurosurgical Society** for 1960-1961: president, Dr. Harold R. Oberhill, Chicago; vice-president, Dr. Peter V. Westhaysen, Hammond, Ind.; and secretary-treasurer, Dr. Luis V. Amador, Chicago.——At the annual meeting of the **American Association for the History of Medicine, Inc.**, Chauncey D. Leake, Ph.D., Galveston, Texas, was elected president and Dr. Lloyd G. Stevenson, Montreal, Canada, was elected vice-president. Officers in the association are elected for a term of two years. There was no election for secretary-treasurer this year.——The American **Radium Society** announced that Dr. Jesshill Love, Louisville, Ky., assumed the president's office from Dr. Theodore R. Miller, New York City, retiring president. Named president-elect was Dr. Robert L.

Brown, Atlanta, Ga. Other officers include Dr. Charles G. Stetson, Englewood, N. J., secretary, and Dr. Gilbert H. Fletcher, Houston, Texas, treasurer. The next annual meeting will be held in Colorado Springs, Colo., May 11-13, 1961.

Doctors' Nurses Convene in Miami.—Doctors' Nurses Day on June 25 has been proclaimed by Governor LeRoy Collins of Florida in honor of the first convention the members of the American Association of Doctors' Nurses. The session will be held on June 23-26 at Hotel Deauville, Miami. A number of medical organizations will furnish speakers and exhibits. Included is a talk by a representative of the American Cancer Society, speaking on "The Importance of Cytology in the Early Detection of Cancer in Women." The Arthritis and Rheumatism Foundation will send a speaker and a display on "Quackery in Arthritis." The Florida Association for Mental Health will provide a speaker and exhibits, and the American Medical Association will loan a part of its exhibits which are of interest to the nurses. Symposiums are planned. Entertainment includes a reception, a boat trip, and a postconvention visit to Nassau and Jamaica. The membership of the American Association of Doctors' Nurses is made up of women who serve in doctors' offices as nursing assistants. The headquarters are in the Farragut Building, Washington, D. C.

Meeting of Genito-Urinary Surgeons.—The American Association of Genito-Urinary Surgeons will hold its 71st annual meeting May 11-13 at the Dearborn Inn, Dearborn, Mich., under the presidency of Dr. Reed M. Nesbit, Ann Arbor, Mich. The following papers include invited authors:

Physiopathology of Stress Incontinence, Dr. Jack Lapides, Ann Arbor.
Vesicourethrography, Dr. Lonnie W. Howerton Jr., Louisville, Ky.
Conservative Treatment Often Successful for Vesico-Ureteral Reflux, Dr. Donn E. Leuzinger, Staten Island, N. Y.
Experiences with Tumors of the Renal Pelvis and Ureter, Dr. Edward C. Parkhurst, Boston.
The Development and Operation of a Dialysis Unit on the Urological Service, Drs. William H. Lakey and Joseph C. Cerny, Ann Arbor.
Retroperitoneal Fibrosis Producing Ureteral Obstruction, Drs. Herman I. Riddell, Louis J. Lombardo Jr., Los Angeles.
Bilateral Cutaneous Ureterostomy, Side by Side, in the Midline for Urinary Diversion, Dr. Richard L. Sallade, Boston.

The annual banquet will be held the evening of May 12. For information, write Dr. William J. Engel, 2020 E. 93rd St., Cleveland 6, Secretary.

Propose Study on Chagas Disease.—A study group on Chagas disease recommended to the Pan American Sanitary Bureau that the organization sponsor studies to determine the magnitude of the problem the disease represents to the hemisphere. In a report issued at the close of a week-long study session held in the bureau's Washington headquarters, experts from Argentina, Brazil, Chile, Mexico, Peru, Venezuela, and the United States said that although about 35 million persons in the Americas were yearly exposed to the disease, some of the basic facts about it are still unknown. They recommended that the bureau sponsor research on its epidemiology, the ecology and susceptibility to residual insecticides of the insect (known as the "kissing bug" in the United States) that spreads it, and better means of both preventing it and of treating persons who suffer cases of it. Chagas disease is found as far north as the United States and as far south as Argentina, principally in rural areas with low standards of housing and sanitation. It was first identified in 1909 by the Brazilian scientist, Dr. Carlos Chagas. So far as is known the disease exists only in the western hemisphere.

Meeting of Cleft Palate Rehabilitation.—The American Association for Cleft Palate Rehabilitation will be held May 12-14 at the Brown Palace Hotel, Denver, with a short course May 12 on the problems associated with the habilitation of individuals with cleft lip and palate which includes the following papers:

Anatomy of the Head and Neck, Dr. Archibald R. Buchanan, Denver.
Physiology of the Head and Neck, Dr. Buchanan.
Pathogenesis of Cleft Lip and Palate, Dr. Josef Warkany, Cincinnati.
Morphogenesis of Cleft Lip and Cleft Palate as Seen in Experimental Animals, Harold Kalter, Ph.D., Cincinnati.
Congenital Dento-Facial Anomalies, Fred M. Deuschle, D.D.S., Cincinnati.

Limited attendance clinics will be held on prosthetics and orthodontic procedures, surgical procedures, and speech procedures, and a discussion, "The Value of Pharyngeal Flap Surgery," will be moderated by Dr. Herbert Conway, New York City, the afternoon of May 13. Films and scientific exhibits are planned. Registration fee for nonmembers is $3. For information, write D. C. Spriestersbach, Ph.D., Department of Otolaryngology, University Hospitals, Iowa City, Iowa, Secretary-Treasurer.

Urology Meeting in Chicago.—The 55th annual meeting of the American Urological Association, Inc., will be held May 16-19, at the Palmer House, Chicago, under the presidency of Dr. Edgar Burns, New Orleans. Two panel discussions are planned: "Ureteral Reflux" and "Pyelonephritis." Dr. Peter Bischoff, chief, department of urology, Elisabeth Hospital, Hamburg, Germany, will present "Origin, Clinical Experiences and Treatment in Urinary Obstructions of the Lower Ureter in Childhood." Dr. Khalil Abi-Torbey, Boston, will present the society's prize essay the morning of May 18 on "Urinary Continence and Normal Urination Provided by Urethral and Sphincter Substitution with a Special Seromuscular Segment of Ileum in Male and Female Dogs." Dr. Burns will present "The Present Day Urologist—His Education and Obligations" as the president's address, and "Another Hopeful Look at Ureterosigmoid Anastomosis" will be presented as the Ramon Guiteras Lecture by Dr. Reed M. Nesbit, Ann Arbor, Mich. The banquet will be held May 18, 8 p. m. Entertainment includes a golf tournament May 16. A ladies' program is arranged. Registration fee is $30 (accompanying ladies $20). For information, write Mr. William P. Didusch, 1120 N. Charles St., Baltimore 1, Executive Secretary.

Society News.—The **American Society for the Study of Sterility** officers are: president, Dr. S. Leon Israel, Philadelphia; president-elect, Dr. Robert B. Wilson, Rochester, Minn.; honorary vice-president, Dr. Georgeanna Seegar Jones, Baltimore; secretary, Dr. Herbert H. Thomas, Birmingham, Ala.; assistant secretary, Dr. William H. Robertson, Birmingham, Ala.; and treasurer, Dr. Melvin L. Taymor, Boston. ——At the annual meeting of the **American Psychosomatic Society** the following persons took office: Dr. Morton F. Reiser, Washington, D. C., president; Dr. Stewart G. Wolf Jr., Oklahoma City, president-elect; and Dr. Eugene Meyer III, Baltimore, secretary-treasurer. The 18th annual meeting of the society will be held on April 29-30, 1961, in Atlantic City, N. J.——At the annual meeting of the **American Epilepsy Society**, Peter E. Kellaway, Ph.D., Houston, Texas, was installed as president, and Dr. William Caveness, of New York City, was chosen as president-elect. Dr. H. Houston Merritt, New York City, represents the society as vice-president for the International League Against Epilepsy. Dr. James W. Crawley, Houston, was reelected treasurer, and Dr. Madison H. Thomas, Salt Lake City, was reelected secretary. The next annual meeting of the society will be held on Dec. 8, in New York City, just prior to the meeting of the Association for Research in Nervous and Mental Diseases.

Fellowships for Heart Research.—Applications from research investigators for support of studies to be conducted during the fiscal year beginning July 1, 1961, are being accepted by the American Heart Association. The deadline for applying for research fellowships and established investigatorships is Sept. 15. Applications for grants-in-aid must be received by Nov. 1. Applications may be made for awards in the following categories: (1) Established Investigatorships: Usually awarded for five years, subject to annual review, in amounts ranging from $7,500 to $9,900 yearly plus dependency allowance, to "scientists of proven ability" who have developed in their research careers to the point where they are independent investigators; (2) Advanced Research Fellowships: Awarded for periods of one or two years to postdoctoral applicants who have had some research training and experience but who are not clearly qualified to conduct their own independent research, stipends range from $5,500 to $6,000 annually, plus dependency allowance; (3) Research Fellowships: Available to young men and women with doctoral degrees for periods of one or two years to enable them to train as investigators under experienced supervision, annual stipends range from $4,000 to $4,500 plus dependency allowances; and (4) Grants-in-Aid: Made to experienced investigators to help underwrite the costs of specified projects, such as equipment, technical assistance, and supplies. Information and application forms may be obtained from the Assistant Medical Director for Research, American Heart Association, 44 E. 23rd St., New York 10.

Mortality Record for 1959.—The Metropolitan Life Insurance Company reports that in 1959 the death rate among the industrial policyholders of the company was fractionally higher than that in the preceeding year, but when allowance is made for the increase in the average age of the insured the mortality record for all ages combined shows a 2% decrease from 1958. In the past three years, mortality has been at a somewhat higher level than in the preceeding three years, reportedly reflecting, in part at least, the widespread prevalence of upper respiratory infections. During 1959, about 108,000 deaths were reported among the company's industrial policyholders at ages of one and over. If the death rates by age in each color-sex group had been the same as those in 1911, there would have been 291,000 deaths among the insured. Each sex recorded a reduction in mortality from 1958 to 1959. Among white males the age-adjusted death rate at ages 1-74 combined fell from 9.27 per 1,000 to 8.95, or 4%. Among white females the death rate decreased from 4.63 to 4.56 per 1,000 and established a new low. Reductions were noted among white males in each age group except 5-19 years, but among white females no distinct age pattern was found. Since 1911-1915 reductions in mortality have occurred at every age period. Heart disease is currently the leading cause of death among the industrial policyholders, accounting for about 40% of the total mortality at all ages combined. The cardiovascular-renal diseases as a whole (including vascular lesions of the central nervous system) were responsible for more than half the mortality from all causes combined. Cancer (malignant neoplasms) accounts from about one death in every five, and accidents for one death in every 20.

Tuberculosis Convention in Los Angeles.—The National Tuberculosis Association, the American Trudeau Society, and the National Conference of Tuberculosis Workers will hold their annual meetings simultaneously at the Statler Hilton Hotel, Los Angeles, May 15-19. The program includes public health, nursing, business, special interest, and medical sections, and the latter will include the following seminars and moderators:

Practical Pulmonary Function Testing, Dr. John Kiernan, Oakland, Calif.
Compulsory Isolation of the Recalcitrant Patient, Dr. Joseph B. Stocklen, Cleveland.
Treatment of the Chemotherapy Failure, Dr. Paul T. Chapman, Detroit.
Air Pollution and Pulmonary Diseases, Dr. Herman Gierson, Los Angeles.
Treatment of Bone and Joint Tuberculosis, Dr. Abraham Falk, Minneapolis.
Indications for Lung Collapse, Dr. Norman J. Wilson, Boston.
Surgery of Lung Cancer—How Much? Dr. John C. Jones, Los Angeles.
Treatment of Empyema, Dr. Paul C. Samson, Oakland, Calif.

To open the general session May 16, Senator Lister Hill, of Alabama, will present the keynote address. Dr. Sidney Raffel, Stanford, Calif., will present the Amberson Lecture the morning of May 17, entitled "Aspects of Contemporary Research in Immunology." A symposium, "Current Cooperative Studies in Lung Cancer Chemotherapy, Including Experimental Methods and Results," will be moderated by Dr. C. Gordon Zubrod, Bethesda, Md., the afternoon of May 18. Demonstrations are planned and a case conference is scheduled for the afternoon of May 17. For information, write Mr. Frank W. Webster, 1790 Broadway, New York 19. Executive Secretary, American Trudeau Society.

CANADA

Psychiatry Congress in Montreal.—On June 4-10, 1961, the third World Congress of Psychiatry will be held in Montreal under the auspices of the International Psychiatric Association and McGill University Faculty of Medicine, Montreal, Quebec, Canada. The program is planned to include three general categories as follows: (1) Phenomenological—Observational, (2) Experimental—Therapeutic, (3) Interpretive—Theoretical. Suggested areas of special interest include animal behavior, genetics, constitution, development, ethology, child psychiatry, adult psychiatry, group behaviour, geriatrics, and studies using basic science methodology. Persons wishing to present papers should contact the General Secretary, Dr. Charles A. Roberts, Allan Memorial Institute, 1025 Pine Ave., West, Montreal 2, P. Q., Canada, by Sept. 1. Abstracts must be mailed in time to reach the General Secretary not later than Dec. 1. They should not exceed 250 words. Film exhibits and postcongress tours are planned.

LATIN AMERICA

Post-Convention Conference in Cuba.—A clinical conference sponsored by the Cuban Medical Association at the Cuban Medical National College Building, Havana, will be held June 18-21, following the A. M. A. convention in Miami Beach, Fla. Among the papers to be presented is "Practical Gynecology" an illustrated presentation by Drs. Mitchell J. Nechtow, Chicago, and Walter J. Reich, Highland Park, Ill. For information, write Dr. Pedro A. Valdes, 3203 W. North Ave., Chicago 47.

FOREIGN

Bureau to Aid Medical Visitors in England.—The Council of the British Medical Association established an International Medical Advisory Bureau with a view toward welcoming and providing a personal advisory service to medical practitioners visiting the United Kingdom. The bureau is located at British Medical Association House, Tavistock Square, London, W.C. 1. One object of the bureau is to welcome the overseas medical visitor, who is invited to visit the bureau as soon as possible after arrival and talk over with the medical director any points on which he may need advice or assistance. Information is available on postgraduate education facilities, and visits to hospitals and clinics can be arranged. Assistance will be given in finding suitable hotel and lodging accommodations. General information on cars, sports, traveling, exhibitions, theaters, etc., is available. Visitors are urged to inform the bureau of any intended visit to the United Kingdom as much in advance of arrival as possible. All communications should be sent to the Medical Director, International Medical Advisory Bureau, Tavistock Square, London, W.C. 1, England.

Congress on Prophylactic Medicine.—The Congress of Prophylactic Medicine and Social Hygiene in Bad Aussee, Austria, Aug. 29-Sept. 5, 1959, reportedly was received so well that the delegates of 14 countries (U. S. A., England, Germany, Belgium, Russia, Italy, Hungary, Spain, Austria, Denmark, Romania, Yugoslavia, Switzerland, and Greece) decided to organize another world congress in Bad Aussee Sept. 3-10, 1960. The main themes of discussion will be as follows:

1. Prevention of Importation of Intercontinental Infectious Diseases.
2. State of Campaign Against Poliomyelitis in Various Countries.
3. Preventive Measures Against the Risks of Irradiation.
4. Support Given to Working Mothers.
5. Problems of Geriatric Hygiene from the Mental Point of View.
6. Industrial Medicine.
   (a) Campaign Against Noise; (b) Prophylaxis of Dermatoses Caused by Working Conditions.
7. Bioclimatology and Physical Medicine in Their Significance for Prophylaxis.
8. Free Discussions.

For information, write the Secretary General Dr. E. Berghoff, VIII, Piaristengasse 41, Vienna, Austria.

Symposium on Lipid Metabolism.—On June 2-4, an International symposium, "Drugs Affecting Lipid Metabolism," will be held in Milan, Italy, at the auditorium of the Pirelli Center. The scientific program includes reports to be presented on the following major topics:

- Recent Data on the Metabolism of Cholesterol and of Lipids.
- Experimental Methods for Appraising Drugs Affecting the Metabolism of Cholesterol and of Lipids.
- Drugs Affecting the Metabolism of Cholesterol and Lipids in Relation to the Prevention and Treatment of Experimental Atherosclerosis.
- Clinical Practice and the Therapeutical Value of Drugs Affecting the Metabolism of Cholesterol and of Lipids.

A meeting and informal discussion on the present status of gas chromatography will be held. The official languages will be Italian and English, with simultaneous translations available in Italian, English, French, and German. A scientific display of equipment and techniques is planned. A program of official ceremonies and other entertainment is arranged. For information, write the Secretary, Prof. Silvio Garattini, % Istituto di Farmacologia dell'Universita, Via A Del Sarto 21, Milan, Italy.

CORRECTIONS

Officers.—In the April 16 issue of THE JOURNAL, page 1719, an error appears in the spelling of the name of the Vice-president, J. Stanley Kenney.

Amphetamine, Secobarbital, and Athletic Performance.—In the contribution by Drs. Smith and Beecher entitled "Amphetamine, Secobarbital, and Athletic Performance" appearing in THE JOURNAL, April 2, pages 1502-1514, there is an error in table 2, page 1504. The next-to-last column is headed "S=P." It should read "P>S."

EXAMINATIONS AND LICENSURE

MEDICAL SPECIALTY BOARDS

American Board of Anesthesiology: *Written.* Various locations, June 24. Final date for [illegible] was January 10. Sec., Dr. Forrest E. L[illegible], [illegible]rmington Ave., Hartford 5, Conn.

American Board of Dermatology: Final date for filing applications of candidates completing training by October 15, 1960 is March 1, 1961. *Written.* Several cities, June 5, 1961. *Oral.* Philadelphia, Oct. 13-16, 1961. Sec., Dr. Beatrice M. Kesten, One Haven Avenue, New York 32, New York.

American Board of Internal Medicine: New York City, Nov. 14-17. Closing date for filing application is July 1. *Written.* Oct. 17. Closing date for filing application was May 1. Sec.-Treas., Dr. William A. Werrell, One West Main St., Madison 3, Wis.

American Board of Neurological Surgery: Examination given twice annually, in the spring and fall. In order to be eligible a candidate must have his application filed at least six months before the examination time. *Oral.* New Haven, Nov. 6-9. Sec., Dr. Donald D. Matson, 300 Longwood Ave., Boston, Mass.

American Board of Obstetrics and Gynecology: Applications for certification in Part I, new and reopened, and requests for reexamination in Part II are now being accepted. Deadline for receipt of applications is August 1, 1960. After July 1, 1962, a minimum of three years of approved progressive residency training will be required. Training by preceptorship will no longer be acceptable. The initiation of preceptorships will not be approved after July 1, 1960. Sec., Dr. Robert L. Faulkner, 2105 Adelbert Road, Cleveland 6.

American Board of Ophthalmology: *Written.* Jan. 23, 1961. Deadline for filing applications is July 1. *Oral.* Chicago, Oct. 3-7. Sec., Dr. Merrill J. King, Box 236 Cape Cottage Branch, Portland, Maine.

American Board of Orthopaedic Surgery: *Oral and Written, Part II.* Miami Beach, Jan. 3-5, 1961. Final date for filing application is July 1. Sec., Dr. Sam W. Banks, 116 South Michigan Ave., Chicago 3.

American Board of Otolaryngology: *Oral,* Chicago, Oct. 3-6. Final date for filing application was April 1. Sec., Dr. Dean M. Lierle, University Hospitals, Iowa City.

American Board of Pediatrics: *Written.* New York City, January 1961. Final date for filing application is Dec. 1. Administrative Sec., Mrs. Eleanor J. Mitchell, Rosemont, Pa.

American Board of Physical Medicine and Rehabilitation: *Oral and Written.* New York, June 17-18. Sec., Dr. Earl C. Elkins, Mayo Clinic, Rochester, Minn.

American Board of Proctology: *Oral and Written, Parts I and III,* Philadelphia, Sept. 24. Final date for filing application is June 30. Sec., Dr. Stuart T. Ross, 520 Franklin Ave., Garden City, N. Y.

American Board of Psychiatry and Neurology: New York, New York, Dec. 12-13, New Orleans, Mar. 20-21, 1961. Sec., David A. Boyd, Jr., 102-110 Second Ave., S.W., Rochester, Minn.

American Board of Radiology: *Examination.* Cincinnati, June 6-10; Dec. 10-13. Deadline for filing applications for the June examination was Jan. 1. Filing deadline for the December examination is July 1. A special examination in Nuclear Medicine (for those diplomates in Radiology or Therapeutic Radiology) will be offered provided there are sufficient applications. Sec., Dr. H. Dabney Kerr, Kahler Hotel Bldg., Rochester, Minn.

American Board of Surgery: *Written.* (Part 1), Various Centers, Dec. 7. *Candidates are urged to apply several months before completion of training requirements.* The closing date for filing applications is August 1. Those completing training requirements after September 30 cannot be considered for the December Part I examination of the same year. *Oral.* (Part II)—New Haven, Sept. 26-27; Indianapolis, Oct. 24-25; Buffalo, Nov. 14-16; Nashville, Dec. 12-13; Philadelphia, Jan. 16-17; Houston, Feb. 13-14; Columbus, Ohio, Mar. 13-14; New York City, April 19-20; Portland, Ore., May 15-16; San Francisco, May 18-19. No examinations will be held in June, July or August. Sec.-Treas., Dr. John B. Flick, 1617 Pennsylvania Blvd., Philadelphia 3.

Board of Thoracic Surgery: *Written.* Various centers throughout the country, Sept. 9. Final date for filing application is July 1. *Oral.* Oct. 1960. Final date for filing application is July 1. Sec., Dr. Wm. M. Tuttle, 1151 Taylor Ave., Detroit 2.

American Board of Urology: *Written.* December. *Oral-Clinical.* Chicago, February 1961. Exec. Sec., Mrs. Ruby L. Griggs, 30 Westwood Road, Minneapolis 26.

GOVERNMENT SERVICES

FEDERAL AVIATION AGENCY

Bureau of Aviation Medicine Established.—The Federal aviation Agency has established a new bureau of Aviation medicine to replace the former office of the civil air surgeon. The elevation to bureau status points up the growing significance of the role of the medical program in the agency's primary mission of air safety. The new bureau will be headed by Dr. James L. Goddard, who will retain his present title of civil air surgeon. The bureau of aviation medicine will retain an organizational structure similar to its predecessor and will be made up of the civil air surgeon's office and the following four divisions: research requirements, medical standards, medical certification, and environmental health.

The functions of the bureau of aviation medicine include responsibility to promote safety by developing standards and regulations concerning the mental and physical fitness of airmen as well as all others whose health affects safety in flight. This includes administration of examinations, inspection, and certification programs related to such standards and regulations. The bureau is charged with the development of plans for research required in any aspect of medicine affecting civil aviation and supervises all medical research undertaken by the FAA. A third major area is responsibility for providing the medical standards or approval for those design elements of aircraft, aircraft components, and operational procedures which involve medical considerations. A new and growing responsibility is participation in the investigation of the medical aspects of civil aircraft accidents.

FOOD AND DRUG ADMINISTRATION

Food Seizures.—Forty-five tons of canned tomatoes and tomato purées were seized in 10 actions alleging contamination by spoiled tomatoes, fly eggs, and maggots. A total of 168 tons of unfit foods were removed from the market in February. Thirty tons of flour contained live insects, insect parts, and rodent contamination. Rotten eggs in 30-lb. cans of frozen whole eggs intended for sale to food processors caused the seizure of 25 tons. Ten shipments of nuts totaling 12 tons contained live insects, mold, spoilage, and empty shells. In five of the eight actions involving foods in warhouses, the government charged the foods were stored under unsanitary conditions permitting rodent and insect contamination. Ten tons of warehoused flour, rice, cornmeal, dried beans, and nuts were removed from the market. Foods alleged to be hazards to health included malting barley in which seed barley treated with a mercury compound was mixed, Bibb (open leaf) lettuce contaminated with a pesticide (pentachloronitrobenzene) not permitted on lettuce, and 10,000 tablets of a food supplement containing less vitamin A than was declared on the label.

Penalties for Food Adulterations Upheld.—A convicted food warehouseman's contention that he had committed only one offense in storing numerous lots of a variety of foods under unsanitary conditions that caused them to become adulterated was rejected by the federal court for the eastern district of Kentucky. The court held that each lot of food is a separate article and that the adulteration of four different articles of food constituted four separate, distinct violations of the act for which separate penalties might be imposed. Justin M. Schneider, doing business as Central Sales, Covington, Ky., was convicted by a jury under an indictment charging a second violation involving unsanitary food storage, this one causing four separate lots of food to become adulterated. The Court had fined him $750 on each count or a total of $3,000. This sentencing was affirmed by the court in denying the defense motion that three of the $750 fines be vacated and that the defendant be required to pay only one fine.

Government Loses Deceptive Packaging Case.—A court contest of the seizure of chocolate-covered thin mints that the government alleged were deceptively packaged was decided in favor of the Delson Candy Company of New York City. The federal court in February held that the government failed to prove the containers for "Delson Thin Mints" were so made, formed, or filled as to mislead the purchaser as to the number of mints contained in these packages. The government took the position that it did not expect or require that a container would have its interior volume completely filled by pieces of candy but it alleged that the Delson package was misleading and thus misbranded because two hollow dividers between each section of candy and one hollow divider at each end used up available space in the container so that the candy occupied only about 45% of the volume of the package. The federal court, in its opinion, placed great weight on the candy firm's testimony that the particular type of package was needed to prevent breakage of the mints during machine filling, handling, and shipping.

DEATHS

Anderson, Earl Willie, Atlanta, Ga.; Medical Department of Tulane University of Louisiana, New Orleans, 1907; for many years a medical missionary in Korea; died March 4, aged 80.

Baker, George Iverson Ⓜ Staten Island, N.Y.; Jefferson Medical College of Philadelphia, 1926; member of the Industrial Medical Association; died in the Beekman–Downtown Hospital, New York City, March 7, aged 62.

Ball, Robert Samuel, Lebanon, Ind.; Northwestern University Medical School, Chicago, 1925; veteran of World Wars I and II; past-president of the Boone County Medical Society; died in the Methodist Hospital, Indianapolis, March 2, aged 60, of carcinoma.

Brewster, Margaret Powell Ⓜ Elsinore, Calif.; Cornell University Medical College, New York City, 1901; for many years on the staff of St. Luke's Hospital in New York City; died March 6, aged 87.

Bridges, Egbert Cleveland, Donalsonville, Ga.; Louisville (Ky.) Medical College, 1906; died Jan. 29, aged 73.

Britenstool, Harry Ⓜ New York City; Columbia University College of Physicians and Surgeons, New York City, 1901; chief medical consultant at St. Clare's Hospital; one of the founders of the Hospital for Joint Diseases, where he was a medical consultant; died March 8, aged 84.

Butler, Lester Emmons Ⓜ Taunton, Mass.; Boston University School of Medicine, 1904; past-president of the Bristol North District Medical Society; associated with the Morton Hospital, where he was past-president of the staff, and where he died March 4, aged 81.

Carey, Lewis Marshall Ⓜ New Smyrna Beach, Fla.; Michigan College of Medicine and Surgery, Detroit, 1906; veteran of the Spanish–American War; died in the Veterans Administration Hospital, Lake City, March 1, aged 82.

Coleman, Robert Henry Ⓜ North Little Rock, Ark.; Tulane University School of Medicine, New Orleans, 1914; veteran of World Wars I and II; formerly associated with the regional office of the Veterans Administration in Little Rock and since October, 1958, associated with the Veterans Administration Hospital in North Little Rock; died in the Arkansas Baptist Hospital Feb. 28, aged 68, of injuries received in an automobile accident.

Crawford, Sidney Robert, North Little Rock, Ark.; University of Arkansas School of Medicine, Little Rock, 1917; veteran of World War I; during World War II and the Korean War was a medical officer in the induction center in Little Rock; where for many years he was associated with the Veterans Administration; died in Little Rock March 2, aged 66.

Curtiss, Edgar John, Columbus, Ga.; Toledo Medical College, 1910; formerly practiced in Lima, Ohio, serving as coroner of Allen County; veteran of World War II; died Feb. 28, aged 75.

Damstra, Harold James Ⓜ Grand Rapids, Mich.; Northwestern University Medical School, Chicago, 1929; veteran of World War II; associated with the Blodgett Memorial Hospital and the Butterworth Hospital, where he died Feb. 26, aged 57.

Dandrea, Peter Paul Ⓜ Clovis, N. M.; Hahnemann Medical College and Hospital of Philadelphia, 1947; member of the American Academy of General Practice; certified by the National Board of Medical Examiners; interned at the Memorial Hospital in Wilmington, Del.; an officer in the medical corps of the U. S. Army Reserve from 1951 to 1953; a member of the staff of the Memorial Hospital; died in the Colorado General Hospital, Denver, Feb. 28, aged 47, of leukemia.

Davis, Howard Benjamin F. Ⓜ Downingtown, Pa.; University of Pennsylvania School of Medicine, Philadelphia, 1917; fellow of the American College of Surgeons; past-president of the Chester County Medical Society; served as a member of the board of directors of Embreeville (Pa.) State Hospital; associated with the Marshall Square Sanitarium and the Chester County Hospital in West Chester, where he died March 3, aged 65.

Dearborn, Frederick Myers, New York City; New York Homeopathic Medical College and Hospital, New York City, 1900; member of the American Academy of Dermatology and Syphilology; veteran of the Spanish–American War and World War I; served on the faculty of his alma mater, where he was a trustee; associated with the New York Medical College, Flower and Fifth Avenue Hospitals and the Metropolitan Hospital; died Jan. 25, aged 83, of metastatic carcinoma of the colon to liver and lung.

Devlin, John James, New York City; New York Medical College, Flower and Fifth Avenue Hospitals, New York City, 1957; interned at the New Rochelle (N. Y.) Hospital; served a residency at the

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Ⓜ Indicates Member of the American Medical Association.

Bird S. Coler Hospital-Home; certified by the National Board of Medical Examiners; killed March 14, aged 30, in an automobile accident.

Dingman, Marshal Edwin Ⓜ Urbana, Iowa; State University of Iowa College of Médicine, Iowa City, 1902; at one time served as a member of the school board; member of the staffs of St. Luke's Methodist Hospital and the Mercy Hospital, Cedar Rapids, where he died March 1, aged 80.

Fischer, Herman Adam Ⓜ Wilkes-Barre, Pa.; University of Pennsylvania Department of Medicine, Philadelphia, 1900; fellow of the American College of Surgeons; past-president of the Luzerne County Medical Society; associated with the Nesbitt Memorial Hospital in Kingston; died March 8, aged 82.

Frazier, James Wood Ⓜ Charleston, W. Va.; Medical College of Virginia, Richmond, 1928; died March 11, aged 62.

Frisbie, Frank Chester Ⓜ Equinunk, Pa.; University of Vermont College of Medicine, Burlington, 1898; past-president of the Wayne, Pike Counties Medical Society; for many years on the staff of the Carbondale (Pa.) General Hospital; in 1948 honored by the Medical Society of the State of Pennsylvania and presented with a plaque for 50 years outstanding service; died Feb. 26, aged 90.

Gallagher, Robert Paul Ⓜ Amarillo, Texas; University of Minnesota Medical School, Minneapolis, 1943; interned at the Queen's Hospital in Honolulu, Hawaii; veteran of World War II; at one time editor of the *Bulletin of Potter-Randall County Medical Society;* served on the staff of the Veterans Administration Hospital, where he died March 5, aged 45, of multiple sclerosis.

Green, Seibels Remington Jr., Lima, Ohio; Meharry Medical College, Nashville, Tenn., 1943; interned at the Homer G. Phillips Hospital in St. Louis; served a residency at the Kansas City General Hospital in Kansas City, Mo.; formerly an officer in the U. S. Air Force Reserve; member of the Aero Medical Association; associated with the Lima Memorial Hospital and the St. Rita's Hospital, where he died March 1, aged 40.

Green, William Wills, Tarboro, N. C.; University of North Carolina School of Medicine, Chapel Hill, 1908; for many years chairman of the county board of education; past-president of the Edgecombe-Nash Counties Medical Society; fellow of the American College of Surgeons; chief of Staff at Edgecombe General Hospital; veteran of World War I; physician to the Edgecombe Draft Board during World War II; past-member of the county board of health; died in the Duke Hospital, Durham, March 5, aged 74.

Hemond, Fernand Joseph, West Warwick, R. I.; Laval University Faculty of Medicine, Quebec, Que., 1931; served as district medical examiner; died in St. Joseph's Hospital, Providence, March 1, aged 56.

Howard, Robert Lowe Ⓜ Spokane, Wash.; Western Reserve University School of Medicine, Cleveland, 1928; *specialist certified by the American Board of* Dermatology; member of the American Academy of Dermatology and Syphilology; past-president of the Pacific Northwest Society of Dermatologists; associated with the Deaconess, Sacred Heart and St. Luke's hospitals; dermatologist consultant at the Veterans Administration Hospital; editor of the *Bulletin of the Spokane County Medical Society;* died Feb. 25, aged 62.

Jacques, William Addison Ⓜ Fort Lauderdale, Fla.; Fordham University School of Medicine, New York City, 1917; veteran of World Wars I and II; served in the regular Army; formerly chief medical officer for the Veterans Administration Regional Office in Philadelphia; practiced in Ashland, Pa., where he was associated with the Ashland State Hospital; died in the North Broward General Hospital Feb. 20, aged 67, of pneumonia.

Johnson, Fenimore Stratton Ⓜ Commander, U. S. Navy, retired, Ventnor, N. J.; University of Pennsylvania School of Medicine, Philadelphia, 1917; served in the U. S. Navy from 1917 to 1942 when he retired; died in the U. S. Naval Hospital, Philadelphia, Feb. 27, aged 68.

Johnson, Karl Frederick, St. Paul; University of Minnesota Medical School, Minneapolis, 1932; died Feb. 26, aged 52.

Johnston, Marius Early Ⓜ Lexington, Ky.; Columbia University College of Physicians and Surgeons, New York City, 1903; died March 5, aged 80.

Jolma, Keijo Kullervo Ⓜ Gardner, Mass.; Tufts College Medical School, Boston, 1931; fellow of the American College of Surgeons; past-president of the Worcester North District Medical Society; veteran of World War II; on the staff of the Heywood Memorial Hospital; died March 1, aged 52.

Jungk, Carl George Washington Ⓜ St. Louis; Washington University School of Medicine, St. Louis, 1903; served on the staffs of the Deaconess and St. Anthony hospitals; died in the City Hospital Feb. 6, aged 83, of arteriosclerosis.

Kane, R. Emmet Ⓜ St. Louis; Washington University School of Medicine, St. Louis, 1899; in 1939 member of the House of Delegates of the American Medical Association; past-president of St. Louis Medical Society; from 1916 to 1920 professor of medical jurisprudence in the law department at St. Louis University; in 1949 appointed to the Order of Knights of St. Gregory by Pope Pius XII; past-president of the Washington University Alumni Association; associated with the De Paul Hospital, where he died March 1, aged 82.

Katz, Samuel Herschel Ⓜ Philadelphia; Hahnemann Medical College and Hospital of Philadelphia, 1936; also a graduate in pharmacy; district medical supervisor for the board of education; veteran of World War II and was awarded the Purple Heart; associated with the Albert Einstein Medical Center Northern Division and St. Luke's and Children's Medical Center; died in the Albert Einstein Medical Center Northern Division March 3, aged 50, of myocardial infarction.

Katzenstein, Alfred Moses, New York City; Georg August-Universität Medizinische Fakultät, Göttingen, Prussia, Germany, 1905; died March 11, aged 79.

Kemmerly, Harry Paul Ⓜ Tulsa, Okla.; University of Arkansas School of Medicine, Little Rock, 1928; member of the American Society of Anesthesiologists; on the staff of the Hillcrest Medical Center; died Feb. 29, aged 58.

Kemp, Paul Sadler Ⓜ Macon, Ga.; Medical College of Georgia, Augusta, 1933; interned at the University Hospital in Augusta, where he served a residency; veteran of World War II; died in Atlanta Feb. 23, aged 50.

Kempter, Julius Elmond Ⓜ Chambersburg, Pa.; University of Maryland School of Medicine, Baltimore, 1894; past-president of the Franklin County Medical Society; member of the staff of the Chambersburg Hospital; died in the Williamsport (Md.) Sanitarium March 4, aged 92.

Kent, A. Richard, Springfield, Ohio; New York Homeopathic Medical College and Flower Hospital in New York City, 1915; past-president of the Clark County Medical Society; associated with the Mercy Hospital and the City Hospital, where he died Feb. 18, aged 70, of cancer.

Knapp, Richard Edward Ⓜ Hackensack, N. J.; Columbia University College of Physicians and Surgeons, New York City, 1907; fellow of the American College of Physicians; member of the Radiological Society of North America; veteran of World War I; associated with the Hackensack Hospital; served as a director of the City National Bank of Hackensack; died March 9, aged 75.

Knott, Robert Church Ⓜ Eugene, Ore.; Albany (N. Y.) Medical College, 1928; member of the American Academy of General Practice; a past-secretary and a member of the executive board of the Oregon Academy of General Practice; veteran of World War II; on the staff of the Sacred Heart Hospital; died Feb. 26, aged 59.

Kupperman, Moses Ⓜ New York City; Long Island College Hospital, Brooklyn, 1917; member of the American Academy of General Practice; died in the Beth Israel Hospital March 10, aged 64.

Kuznitzky, Erich, New York City; Schlesiche-Friedrich-Wilhelms Universität Mediziniche Fakultät, Breslau, Prussia, Germany, 1912; associated with the Beekman-Downtown and Fordham hospitals; died March 1, aged 76, of pulmonary embolism.

Landrum, Albert Brewer Ⓜ Columbus, Ohio; Ohio Medical University, Columbus, 1906; specialist certified by the American Board of Urology; member of the American Urological Association; at one time on the faculty of the Ohio State University College of Medicine; associated with the St. Anthony's, White Cross, Grant, and Mercy hospitals; died in El Paso, Texas, March 5, aged 76.

Langhorst Henry Frederick Ⓜ Coral Gables, Fla.; Vanderbilt University School of Medicine, Nashville, Tenn., 1898; veteran of World War I; formerly practiced in Elmhurst, Ill., where he was associated with the Memorial Hospital of Du Page County; died Feb. 14, aged 84.

Larson, Tom Kimber Ⓜ Warren, Pa.; Temple University School of Medicine, Philadelphia, 1930; past-president of the Warren County Medical Society; died in the Warren General Hospital March 7, aged 56.

Laughlin, John, Bedford, Ind.; Medical College of Indiana, Indianapolis, 1892; served Bedford city schools as a member of the school board; died in the Dunn Memorial Hospital March 2, aged 92.

Lenz, Herman John Ⓜ Seattle; Washington University School of Medicine, St. Louis, 1904; served on the staff of the Columbus Hospital; died Feb. 19, aged 79, of bronchopneumonia.

Levine, Abraham Morris Ⓜ Boston; Tufts College Medical School, Boston, 1923; died in the Beth Israel Hospital Feb. 24, aged 60.

Lewellen, Jesse Deleon, San Diego, Calif.; Medical College of South Carolina, Charleston, 1898; veteran of World War I; died Feb. 27, aged 87.

Linch, Albert Osborn Ⓜ Atlanta, Ga.; Emory University School of Medicine, Atlanta, 1925; member of the Southeastern Surgical Congress; fellow of the American College of Surgeons; veteran of World War II; past-president of the Fulton County Medical Society; associated with the Grady Memorial, Emory University, Crawford W. Long Memorial, and Georgia Baptist hospitals; died Feb. 26, aged 58.

Lippman, Emanuel Shalet Ⓜ Minneapolis; University of Minnesota Medical School, Minneapolis, 1929; specialist certified by the American Board of Pediatrics; member of the American Academy of Pediatrics; veteran of World War II; clinical assistant professor of pediatrics at his alma mater; served on the staffs of Abbott Hospital and Mount Sinai Hospital; died Feb. 24, aged 54.

McCarthy, Robert Kenneth, Hanover, Mass.; Tufts College Medical School, Boston, 1957; interned at the Boston City Hospital; served a residency at the Veterans Administration Hospital in Boston; certified by the National Board of Medical Examiners; died in Boston Feb. 21, aged 29, of leukemia.

McClintock, Francis Blake, Saugus, Mass.; Harvard Medical School, Boston, 1904; served on the staff of the Chelsea (Mass.) Memorial Hospital; died in the Massachusetts General Hospital, Boston, March 1, aged 79.

McCormack, Myron Thomas Ⓜ Milwaukee; Marquette University School of Medicine, Milwaukee, 1935; member of the American Academy of General Practice; veteran of World War II; on the staff of the Misericordia Hospital; died March 18, aged 50.

MacKay, Hunter John Ⓜ Seattle; born in Cleveland April 26, 1911; Western Reserve University School of Medicine, Cleveland, 1937; interned at the Providence Hospital; served a fellowship in neurosurgery at the Mayo Foundation in Rochester, Minn.; specialist certified by the American Board of Neurological Surgery; for a time professor of anatomy at Seattle University; member of the Congress of Neurological Surgeons and the Harvey Cushing Society; fellow of the American College of Surgeons; veteran of World War II; associated with the Providence, Swedish, and the Children's Orthopedic hospitals in Seattle and the Northern Pacific Hospital in Tacoma; died March 2, aged 48, of acute pulmonary edema.

MacLean, Louise, Quincy, Mass.; College of Physicians and Surgeons, Boston, 1912; formerly physician at the Lancaster School for Girls in Lancaster; died in the Quincy City Hospital Feb. 17, aged 83.

McMillen, Charles F., Covington, Ky.; Hospital College of Medicine, Louisville, 1898; died in St. Elizabeth Hospital Feb. 21, aged 87.

McNary, John Foster Ⓜ Milwaukee; Wisconsin College of Physicians and Surgeons, Milwaukee, 1906; died March 8, aged 80.

Macnieski, Henry Francis, Harrison, N. J.; Temple University School of Medicine, Philadelphia, 1929; physician for the Harrison Board of Education and Board of Health; served on the staffs of the St. Michael's Hospital in Newark and West Hudson Hospital in Kearney; died March 11, aged 60.

Malinowski, John Joseph Ⓜ Nanticoke, Pa.; Temple University School of Medicine, Philadelphia, 1926; member of the American Academy of General Practice; formerly practiced in Jersey City, where he was member of the staff of St. Francis Hospital; died March 2, aged 58.

Mandl, Gustav Ⓜ Long Island City, N. Y.; Medizinische Fakultät der Universität, Vienna, Austria, 1924; died March 1, aged 62, of coronary thrombosis.

Mathews, William Francis, Woodside, N. Y.; Long Island College Hospital, Brooklyn, 1904; died in the Physicians Hospital, Jackson Heights, March 14, aged 79.

Mecom, W. A., Hebert, La.; Memphis (Tenn.) Hospital Medical College, 1901; for many years practiced in Wisner; died in Jackson Jan. 17, aged 83.

Meltzer, Samuel Louis Ⓜ Portsmouth, Ohio; Boston University School of Medicine, 1925; specialist certified by the American Board of Radiology; fellow of the American College of Radiology; past-president of the Scioto County Medical Society and the Central Ohio Radiological Society; veteran of World War II; at one time on the faculty of the University of Michigan Medical School in Ann Arbor; a consultant of the medical department of the Norfolk & Western Railway; died in the Mercy Hospital Feb. 26, aged 58, of cancer.

Metz, Louis Frederick Ⓜ Stamford, Texas; Vanderbilt University College of Medicine, Nashville, Tenn., 1924; veteran of World War I; physician for the Stamford High School football team; associated with the Stamford Sanitarium; a member of the board of directors of the First National Bank; died Feb. 22, aged 60, of coronary thrombosis.

Miller, Rudolph Richard, Tonawanda, N. Y.; American Medical Missionary College, Battle Creek, Mich., and Chicago, 1903; veteran of World War I; died in the Veterans Administration Hospital, Buffalo, Feb. 19, aged 87.

Miller, William Campbell Ⓜ Guthrie, Okla. George Washington University School of Medicine, Washington, D. C., 1917; veteran of World War I; died in Tahlequah March 1, aged 69.

Millspaugh, Judson Albert Ⓜ Captain, U. S. Navy, retired, St. George, S. C.; University of Arkansas School of Medicine, Little Rock, 1930; member of the American Academy of General Practice; retired Sept. 1, 1952, from the U. S. Navy; died in Port Wentworth, Ga., March 4, aged 56.

Moodie, Bazil M., Tampa, Fla.; Eastern University School of Medicine, Baltimore, 1913; died Feb. 23, aged 87.

Moore, Chester Clarence, Portland, Ore.; Cooper Medical College, San Francisco, 1904; fellow of the American College of Surgeons; died in the Desert Hospital, Palm Springs, Calif., March 2, aged 82.

Normandin, Louis Adolphus, East Providence, R. I.; Tufts College Medical School, Boston, 1919; retired in 1958 as chief medical officer of the Veterans Administration Regional Office in Providence; veteran of World War II; died in Palm Beach, Fla., Feb. 24, aged 66.

Olds, Bomar Amos Ⓜ College Park, Ga.; Emory University School of Medicine, Atlanta, 1921; died in Atlanta Feb. 26, aged 62.

Pickard, Luther James ⓢ Abilene, Texas; University of Texas School of Medicine, Galveston, 1911; past-president of the Taylor County Medical Society; died in the Hendrick Memorial Hospital March 2, aged 72, of injuries received in an automobile accident.

Portnoy, Martin David, Denver; Université de Genève Faculté de Médécine, Switzerland, 1954; interned at St. Joseph's Hospital and served a residency at the University of Colorado Medical Center; died in the Presbyterian Hospital Feb. 27, aged 35.

Pratt, Thomas R. Jr., Pismo Beach, Calif.; University of Maryland School of Medicine, Baltimore, 1913; died Feb. 29, aged 70.

Price, Killian Adolphus, Hickory, N. C.; University of Virginia School of Medicine, Charlottesville, 1907; died March 2, aged 82.

Reynolds, James Isham, Smithville, Texas; Memphis (Tenn.) Hospital Medical College, 1909; died Feb. 8, aged 83.

Richter, Louis Bacon Saunders ⓢ Yoakum, Texas; University of Texas School of Medicine, Galveston, 1935; member of the American Academy of General Practice; associated with the Huth Memorial Hospital; died Feb. 27, aged 49, of coronary occlusion.

Rogers, Frank E. ⓢ Denver; McGill University Faculty of Medicine, Montreal, Que., Canada, 1897; fellow of the American College of Surgeons; past-president of the American Goiter Association; veteran of World War I; associated with the Colorado General Hospital, St. Luke's Hospital, and the Denver General Hospital, where he served as medical director; died Feb. 27, aged 88.

Rosenheck, Charles, New York City; Columbia University College of Physicians and Surgeons, New York City, 1905; specialist certified by the American Board of Psychiatry and Neurology; member of the American Psychiatric Association; neuropsychiatrist for the induction board for New York City from 1941 to 1946; associated with the Beth Abraham Home for Incurables, Hospital for Joint Diseases, Jewish Memorial Hospital, and the Midtown Hospital; died March 6, aged 80.

Rush, James O. ⓢ Forrest City, Ark.; University Medical College of Kansas City, Mo., 1899; served as secretary of the St. Francis County Medical Society; past-president and charter member of the Forrest City Rotary Club; died Feb. 25, aged 92.

Scott, Kenneth Schurch ⓢ Captain, U. S. Navy, retired, Devon, Pa.; University of Pennsylvania School of Medicine, Philadelphia, 1933; specialist certified by the American Board of Preventive Medicine; member of the Aero Medical Association; veteran of World War II; retired from the regular Navy July 1, 1956; past-president of the Chester County Medical Society and the Health and Welfare Council of Chester County; at one time medical director of the Oakbourne Hospital and on the staff of the Chester County Hospital in West Chester; died Feb. 27, aged 57.

Seltzer, Abraham, New York City; Eclectic Medical College, Cincinnati, 1925; died Feb. 15, aged 60.

Seward, Frederick Whittlesey ⓢ Goshen, N. Y.; New York Homeopathic Medical College and Hospital, New York City, 1898; fellow of the American Psychiatric Association; died March 4, aged 85.

Shipp, John Netherland ⓢ Chattanooga, Tenn.; Tulane University School of Medicine, New Orleans, 1921; interned at the Hillman Hospital in Birmingham, Ala.; died Feb. 24, aged 67.

Sinning, Augustus ⓢ Iowa City, Iowa; State University of Iowa College of Medicine, Iowa City, 1895; died in Wilton Junction Feb. 23, aged 95.

Smith, Edward Mack, Madison, N. J.; Tufts College Medical School, Boston, 1927; died in Hammonton Dec. 27, aged 59, of a heart attack.

Smith, Franklin Calton ⓢ Charlotte, N. C.; Jefferson Medical College of Philadelphia, 1921; specialist certified by the American Board of Ophthalmology; member of the American Academy of Ophthalmology and Otolaryngology; past-president of the North Carolina Eye, Ear, Nose and Throat Society; formerly vice-president of the Medical Society of the State of North Carolina; associated with the Charlotte Eye, Ear, Nose and Throat Hospital; died Feb. 25, aged 65.

Smith, James Waller T. ⓢ Hayes, Va.; University College of Medicine, Richmond, 1905; one of the founders and the first president of the Mid-Tidewater Medical Society; for many years county coroner and later county medical examiner; died Feb. 26, aged 75.

Snyder, Vernon James, Camillus, N. Y.; Syracuse University College of Medicine, 1908; health officer for the town of Camillus; school physician and a physician for the Onondaga County Welfare Department; on the courtesy staff of the Crouse-Irving Hospital in Syracuse, where he died Feb. 24, aged 77.

Stephan, Walter Henry, Bellevue, Wash.; Rush Medical College, Chicago, 1914; formerly vice-president of the Montana State Medical Association; served as physician for the Union Pacific Railroad in Dillon, Mont.; died in Goldsboro, N. C., Feb. 23, aged 72.

Sterling, Russell Rhea Ⓢ Houston, Texas; University of Wisconsin Medical School, Madison, 1927; on the staffs of the St. Joseph's Hospital and the Memorial Hospital, where he died Feb. 27, aged 57.

Sussman, S. Theodore Ⓢ New Rochelle, N. Y.; University and Bellevue Hospital Medical College, New York City, 1935; interned at the Hospital for Joint Diseases in New York City; member of the American Academy of General Practice; died in the Bellevue Hospital, New York City, Feb. 11, aged 48.

Thomason, Eugene Archie Ⓢ Fountain Inn, S. C.; Medical College of South Carolina, Charleston, 1948; interned at the Greenville General Hospital in Greenville, S. C.; served a residency at the Duke Hospital, Durham, N. C.; from 1951 to 1953 an officer in the medical corps of the U. S. Army Reserve; died Feb. 25, aged 34, as the result of fire which destroyed his home.

Turner, Floyd Clinton Ⓢ Boulder Creek, Calif.; Chicago College of Medicine and Surgery, 1916: retired from the U. S. Public Health Service; associated with the Boulder Creek Laboratory; died March 5, aged 70.

Wheelon, Frank E. Ⓢ Lake City, Fla.; University of Minnesota College of Medicine and Surgery, Minneapolis, 1900; formerly practiced in Esmond, N. D., and Minot, N. D., where he served as director of the First District Health Unit; veteran of World War I; died Feb. 23, aged 82.

White, John Edwin, Wakefield, Va.; Medical College of Virginia, Richmond, 1900; retired Baptist minister; died Feb. 24, aged 83.

Whiton, Ross Kittredge, Springfield, Vt.; Harvard Medical School, Boston, 1904; at one time on the staff of the Emerson Hospital in Concord, Mass.; died Feb. 22, aged 81.

Wiedman, Frank, South Lyon, Mich.; University of Michigan Homeopathic Medical School, Ann Arbor, 1908; died Feb. 18, aged 80.

Williams, Paul Swift, Elizabethton, Tenn.; Lincoln Memorial University Medical Department, Knoxville, 1910; veteran of World War I; died in the Veterans Administration Center, Mountain Home, Feb. 19, aged 71.

Williams, Theodore L. Ⓢ Bloomington, Ind.; University of Colorado School of Medicine, Denver, 1934; interned at the Denver General Hospital: physician at the Health Center at Indiana University; served as manager of health and charity in Denver from 1936 to 1941; died Feb. 1, aged 57, of pneumonia.

Wilson, Cloyce, Cincinnati; Eclectic Medical College, Cincinnati, 1913; associated with the Bethesda Hospital, where he died March 1, aged 75, of cerebral hemorrhage.

Wilson, Joseph Lorenzo Ⓢ Lexington, Ky.; Tulane University School of Medicine, New Orleans, 1942; interned at the Baptist Memorial Hospital in Memphis, Tenn.; served a residency at the Veterans Administration Hospital in Fort Lyon, Colo.; veteran of World War II; associated with the Veterans Administration Hospital; died Feb. 26, aged 42.

Wilson, William Stuart Jr. Ⓢ Carrizo Springs, Texas; University of Texas School of Medicine, Galveston, 1943; interned at the Robert B. Green Memorial Hospital in San Antonio; veteran of World War II; died Feb. 3, aged 41.

Wortham, James Tolliver Ⓢ Little Rock, Ark.; born in Waldo, Sept. 10, 1924; University of Arkansas School of Medicine, Little Rock, 1947; interned at the Duke Hospital in Durham, N. C., where he served a residency; formerly a resident at the University Hospital and the State Hospital; specialist certified by the American Board of Internal Medicine; member of the Endocrine Society; associate professor of medicine at his alma mater; from 1956 to 1958 an officer in the medical corps of the U. S. Naval Reserve; associated with the St. Vincent Infirmary, Arkansas Baptist Hospital, and the Veterans Administration Hospital; died Feb. 2, aged 35.

Wyland, Byron Jay Ⓢ Mishawaka, Ind.; Indiana Medical College, School of Medicine of Purdue University, Indianapolis, 1906; Indiana University School of Medicine, Indianapolis, 1909; served as vice-president of the St. Joseph County Medical Society; veteran of World War I; served as secretary of the Mishawaka Board of Health; formerly deputy coroner of St. Joseph County; member and past-president of the staff of St. Joseph Hospital, where he died Feb. 17, aged 76, of myocardial infarct.

Yeates, Hugh Wesley, Ringling, Okla.; Fort Worth (Texas) School of Medicine, 1907; served at the Veterans Administration Hospital in Sulphur; died in Waurika Feb. 2, aged 86.

Yencer, Martin Washington Ⓢ Richmond, Ind.; Central College of Physicians and Surgeons, Indianapolis, 1897; at one time served as state representative from Wayne County; died Feb. 22, aged 88.

Young, James Moses Ⓢ Orion, Ill.; Chicago Medical School, 1933; interned at St. Margaret's Hospital in Hammond, Ind.; member of the American Academy of General Practice; served as president of the Henry County Tuberculosis Association; veteran of World War II; associated with the Lutheran Hospital and Moline Public Hospital in Moline; died Jan. 24, aged 58.

FOREIGN LETTERS

BRAZIL

Estrogenic Insufficiency and Sterility.—Medina and Müller (*Rev. ginec. obst.* 106:5, 1960) studied the records of 400 sterile women, 126 (31.5%) of whom showed an estrogenic deficiency. In 54 of these 126 patients the deficiency was caused by a persistent general insufficiency in the production of estrogens or by a deficient reaction of an effector organ. In the other 72 it was not possible to establish an organic basis. This group of cases included 65 patients with confirmed hypoplasia who were separated into three classes: (1) 18 patients who had marked hypoplasia with inversion of the body-cervix ratio (Meaker's index), 16 of them with estrogenic deficiency revealed by cytological examination or by crystallization of the cervical mucus, 14 with global insufficiency, and 2 with preponderant cervical unresponsiveness; (2) 6 patients who had underdeveloped uterus in marked anteflexion, 4 of them with estrogenic deficiency; and (3) 41 patients who had uterine hypoplasia with a relatively good body-cervix ratio and a normal form of the organ but with a length of less than 6 cm., and 18 with a deficient estrogenic index.

Another group of nine patients presented alterations that, although they could not be classified as of a true uterine hypoplasia, deviated so much from the norm as to warrant special consideration. They were nulliparous women with normal-sized uterus but with an excessively long cervix, the whole organ being in retroversion-flexion. Several patients had previously had a gynecologic operation. They had a predominance of secondary sterility, while the two former groups consisted almost exclusively of patients with primary sterility. Some of them showed a more or less persistent estrogenic deficiency, probably caused by surgical operations. A last group of patients with estrogenic deficiency of an organic basis included two patients with secondary sterility, in whom the estrogenic level had fallen abruptly after a normal delivery or after a miscarriage with severe loss of blood.

There were 72 patients who had a functional estrogenic deficiency. The evaluation of these cases presented a certain difficulty due to the multiplicity of factors interfering with the hormonal secretions, and all the observations had only a temporary value. These 72 patients included 64 with a preponderant estrogenic deficiency, 6 with hypophyso-ovarian insufficiency, and 2 with thyro-ovarian insufficiency. Of the 64 with preponderant estrogenic deficiency, 51 had signs of a diminished ovarian function. There were at least 13 patients (9 with primary sterility) in whom the general hormonal activity was sufficient but who presented a persistent unresponsiveness of the cervix uteri to estrogenic stimuli. This form of local deficiency of responsiveness reacts favorably to intracervical estrogenotherapy.

CANADA

Neonatal Blood Findings.—Low and co-workers (*Canad. M. A. J.* 82:12, 70, and 136, 1960) determined the hemoglobin level and hematocrit reading in a series of 104 neonates born to healthy mothers. In cord blood the mean hemoglobin level was 15.77 Gm. per 100 ml. and the hematocrit reading was 52.9%. In the first hour the mean capillary hemoglobin level was 18.55 Gm. per 100 ml. and the hematocrit reading was 62.35%; at 24 hours the corresponding figures were 17.73 and 58.27. The mean values for the mean corpuscular hemoglobin concentrations varied from 29.54 to 30.2%. A wide range of these hematological values was observed, and, of a number of clinical factors studied, only parity showed an effect on the range; a trend to higher levels was observed in primiparous patients. Reasonable lower limits for this normal range are a cord blood hemoglobin level of 12.5 Gm. per 100 ml. and hematocrit reading of 52% in the first hour, and 14.0 and 48, respectively, at 24 hours.

Little relationship was found between values in cord blood and capillary blood in the first hour or between the capillary blood values in the first hour and at 24 hours. This lack of relationship was probably a result of a rapid shift of fluid from the intravascular to the extravascular space. A number of circulatory adjustments occurred in the normal neonate in the first 24 hours. An immediate hemoconcentration took place in the general circulation, possibly due to an increase in blood pressure. Immediately after delivery there was a stasis in the peripheral vascular circulation of the order of 10%. This peripheral vascular stasis persisted to a limited extent after 24 hours, although it was entirely resolved in some infants by this time. There were no changes of hematological values in the first 24 hours. The variation observed in peripheral blood represented only adjustments of the peripheral vascular circulation.

The items in these letters are contributed by regular correspondents in the various foreign countries.

The mean levels of bilirubin at delivery were 2.0 mg. per 100 ml. and at 24 hours 5.1 mg. per 100 ml. The upper limits of normal are 3.0 at delivery and 10 at 24 hours. There was a variable increase in bilirubin level in the early neonatal period. Although the rate of hemolysis might play a limited role, this was largely a result of the variable capacity of the liver to excrete bilirubin. There was a limited relationship between moderate elevations of the bilirubin level and the occurrence of clinical jaundice.

Penicillin Toxicity.—Boyd and co-workers (*Canad. M. A. J.* 82:195, 1960) found that oral administration of large doses of benzylpenicillin potassium produced vomiting in cats and dogs. The oral median emetic dose expressed as grams per kilogram was 0.88 in the cat and 0.85 in the dog. For benzylpenicillin ammonium it was 0.96 in the cat. Vomiting began within 5 to 45 minutes of the time of intragastric administration and lasted 1 to 5 minutes. Recovery was complete. No residual clinical effects were noted during a month's observation after the emetic challenge. Benzylpenicillin-induced vomiting was not inhibited by premedication with chlorpromazine hydrochloride in cats. The oral median emetic dose was estimated to be about 10% of the retained oral median lethal dose in dogs.

The clinical implication of these findings was that certain patients may be inordinately sensitive to the toxic effects of penicillin, effects which were ordinarily seen only when the dose of retained benzylpenicillin was from 5 to 10 Gm. per kilogram of body weight, 1 Gm. being about 1.5 million units. Signs of penicillin poisoning at these dosage levels included nausea, vomiting, anorexia, oligodipsia, irritability, restlessness, convulsions, blepharitis, diarrhea, glycosuria, albuminuria, oliguria, anuria, myocarditis, and anaphylactic shock. Until now, these signs of penicillin toxicity had been thought of as idiosyncrasies or due to previous sensitization instead of toxic side-effects.

Blast Cells in Leukemia.—An analysis was made of 1,827 consecutive marrow examinations and accompanying hemograms performed by Ibbott and co-workers (*Canad. M. A. J.* 82:358, 1960). They attempted to determine a percentage of leukocytic blast cells in the marrow above which the diagnosis of acute leukemia could be made. The criteria for recognition of a leukocyte as a blast cell were (1) absence of cytoplasmic granulation; (2) large nuclear-cytoplasmic ratio, tendency toward large nuclei, or scant cytoplasm; (3) completely divided nuclear chromatin; (4) recognizable nucleoli; and (5) basophilic cytoplasm.

Marrow blast cell counts greater than 6% were found to constitute strong evidence for the diagnosis of acute leukemia. Marrow blast cell counts in excess of 6% were found in 129 patients and 127 (98%) of these proved to have acute leukemia. The critical count of 6% is of least usefulness in those doubtful cases beginning in infancy and early childhood, because of the marked reactivity of the marrow at that time. The two outstanding exceptions in this series were a case of megaloblastic anemia in a 5-month-old girl, who was successfully treated with folic acid, and a leukemoid reaction, presumably due to an allergen or toxin, that occurred in a 4-week-old boy.

Forty-eight patients had blast cell counts between 2 and 6%, and six of these represented acute leukemia in remission or in an early stage of development. Such marrow blast cell counts, therefore, demand further careful investigation. Marrow cell counts up to 2% allow no specific pathological interpretation, since such counts occur frequently in normal persons as well as in many with hematological disorders.

Cigarette Butt Length and Cancer Death Rate.—A total of 6,428 discarded cigarette butts were collected and measured by Hammond and Wynder (*Canad. M. A. J.* 82:372, 1960) who classified them by type and original length of cigarette, and location, socioeconomic class, and sex of the smoker. The mean length of all the butts was 27.9 mm. This is slightly less than the length reported in the United States (30.9 mm.) but much greater than that reported in England and Wales (18.7 mm.) and in the Netherlands (20.9 mm.). The authors stated that smoke from the first part of a cigarette contains proportionally less tar than smoke from the latter part and, therefore, the amount of tar inhaled increases rapidly with the amount of cigarette smoked. For this reason they suggest that average butt lengths be taken into consideration when estimates are made of the average exposure of various groups to cigarette smoke. The differences in average butt length may partially account for reported differences in lung cancer death rates in various countries and various socioeconomic classes.

Appetite Suppressants.—A study was carried out on 192 adult patients, mainly women, by Le Riche (*Canad. M. A. J.* 82:470, 1960), with four appetite suppressants dispensed initially under four code numbers. The experimental period was six weeks. Three of the drugs were commercially available. Two of them contained amphetamine. The fourth was an experimental amphetamine calmative mixture. Average daily weight losses were in those using (1) 30 mg. of 2-phenyl-tertiary-butylamine as the ion-exchange resin complexes, 0.187 lb.; (2) 12.5 mg. of D- and DL-amphetamine as ion-exchange resin complexes, 0.188 lb.; (3) 15 mg. of dextro-amphetamine sulfate as coated granules, 0.162 lb.; and (4) 20 mg. of D- and DL-amphetamine with 40 mg. of methyl-ortho-tolyl-quinazolone as ion-exchange resin complexes, 0.205 lb. Side-effects varied somewhat; dry mouth was the commonest. The drugs did not increase blood pressures. They were much less effective in producing weight loss in a second course with the possible exception of an amphetamine preparation which was followed by 2-phenyl-tertiary-butylamine resin complex.

INDIA

Hydrogenated Ergot Alkaloids.—Subbu and Murthy (*Current M. Pract.* 3:11 [November] 1959) assessed the relative actions of hydrogenated ergot alkaloids on various animals and conducted a clinical trial with these drugs on normal women, who served as controls, and on women with various gynecologic disorders who were admitted for uterine dilatation and curettage. The compounds tried were ergometrine, methyl ergometrine, dihydroergometrine, and dihydroergotoxine. Ergometrine and methyl ergometrine caused an increase in tone in the gravid and nongravid uterus, but the dihydro compounds varied in their actions. In some species these compounds failed to inhibit uterine tone irrespective of the physiological state.

The action of hydrogenated ergot alkaloids in relieving uterine and cervical spasm was studied on normal women and those with disorders such as dysmenorrhea, incomplete abortion, hydatid mole, and sterility. The alkaloids diluted with 5% dextrose were injected intravenously. Isotonic sodium chloride solution, diluted similarly, was given to the controls. Cervical relaxation, if any, was noticed at intervals of 2, 5, and 10 minutes. Of 12 normal women 10 showed relaxation of the cervix after dihydroergotoxine but 2 failed to respond to this compound as well as to dehydroergometrine. Of eight women who were given dihydroergometrine six responded. Isotonic sodium chloride solution had no effect on any of the 20 controls. Three women started vomiting after being given both the alkaloids, and all showed a generalized fall of blood pressure. The undesirable side-effects disappeared in about one-half hour.

An analysis of the results with these alkaloids in patients with gynecologic disorders showed that of 12 women who received dihydroergotoxine 9 responded well and the rest did not respond to either drug. One developed nausea and vomiting which subsided after 10 minutes. All had a fall of blood pressure; eight received dihydroergometrine, and of these five responded with relaxation of the cervix. In two of the three who failed to respond relaxation occurred after dihydroergotoxine was given. Dihydroergotamine also caused a generalized fall in blood pressure which lasted for about 30 minutes, but no gastrointestinal symptoms were seen. Thus both the dihydro compounds produced appreciable cervical relaxation in human beings irrespective of the physiological and pathological state of the uterus. The fall in blood pressure produced by both the compounds in some measure offset their beneficial effect, but this undesirable side-reaction lasted for only a short while.

Processed Protein Foods for Undernourished Infants.—V. Subrahmanyan and co-workers (*Indian J. Pediat.* 26:406 [November] 1959) stated that the diets of weaned infants and young children belonging to the low income groups of the population are grossly deficient in proteins, certain vitamins, and minerals. These children are usually fed on cooked cereals due to the high cost of milk and other foods that would protect them against disease. Because of the low protein content of cereals and their deficiency in certain essential vitamins and minerals, a high incidence of protein malnutrition and deficiency diseases is seen in these children. The authors studied the effect of a balanced malt food and protein foods of low cost in the diets of these infants.

A series of 54 infants varying in age from 9 to 20 months and belonging to the lower middle class were divided into three groups of 18 each on the basis of the initial height, weight, and nutritional status. A diet survey at the beginning of the experiment showed the pattern of the diets consumed by different children to be similar. The main cereal of the diet was raw milled rice. This was supplemented by a small amount of cow's milk, vegetables, pulses, and bread. In addition to this usual diet, the children in the first two groups were given a daily supplement of 2 oz. of malt and protein food and 1 oz. of sugar, respectively, and the third group, the controls, received 2 oz. of coarsely powdered rice and 1 oz. of sugar. The experiment continued for nine months. The supplementary food was enjoyed by all the children receiving it, and none developed any gastrointestinal disturbance during the experiment.

The control and experimental subjects showed about the same nutritional status at the beginning of the trial. At the end of the experiment increases in height, weight, and hemoglobin level of infants receiving malt food and those receiving protein food, respectively, were significantly greater than those of those in the control group. Of the infants in the two experimental groups 30 showed improvement in nutritional status while none in the control group showed improvement and three of the latter showed some deterioration in their nutritional status. Foods such as milk, meat, eggs, and fish are not within the reach of the low-income groups and for them such inexpensive supplementary items as balanced malt food and low-cost protein foods help to prevent the deficiency diseases.

Partial Albinism.—M. Y. Ansari reported an Indian family with partial albinism (*J. Indian M. A.*, vol 34, Jan. 16, 1960). This condition is inherited as a simple dominant characteristic, and although instances have been reported in Negroes none has previously been reported from India. In this family, of a total of 11 offsprings in four generations, 6 were affected and 5 were normal. No generation escaped, and the affected children were born only to affected parents.

The condition was first noticed in a boy nine years of age who came to the hospital with a fracture of his right leg. He was noticed to have a peculiar distribution of white and dark spots on the skin. Irregular milky white spots were present in light colored skin in addition to dark pigmented patches of varying size scattered all over the body. The body hair was light in color, and the hair of the scalp was mainly light with a few patches of dark hair. The other affected members of the family showed similar features. All were apparently healthy. The unaffected members had a dark skin, the color of the pigmented patches in the affected members. The presence of three shades in the affected members was unusual.

Histochemical Endometrial Changes.—S. M. Shahani and co-workers (*J. Obst. & Gynec. India*, vol. 10, December, 1959) studied the endometriums of 30 women between 18 and 30 years of age whose menstrual periods were regular. They came to hospital mainly for dysmenorrhea, leukorrhea, or backache. Histologically the endometrium was in the early proliferative phase in 6, middle and late proliferative phase in 15, early secretory phase in 5, and late secretory phase in 4. The specimens of endometrium were collected by curettage. Alkaline phosphatase activity was evident in the proliferative changes and reached its peak in the late proliferative stage. The glandular secretions in the proliferative stage showed scanty enzyme activity. The nuclei also showed some enzyme activity in the late proliferative stage.

Only traces of glycogen were present in the early part of this phase but increased in amount in the middle and late proliferative stage and appeared as granules in the basal portion of the gland and surface epithelial cells. The stroma and glandular lumen showed only traces, and none was found in blood vessels. Glycoprotein was found only in traces during the entire proliferative phase. In the early progestational phase the alkaline phosphatase showed maximal activity. The nuclei also in most patients showed positive reaction. The glandular secretions showed a maximal amount of alkaline phosphatase during this stage, while the endothelium of the arterioles also showed a positive reaction, as in the late proliferative stage, and the stroma showed variable amounts.

Glycogen actively showed a steady increase in the early progestational phase. The glandular secretions exhibited moderate activity, and the stroma also showed glycogen infiltration. In the late progestational phase, maximal changes were seen. The alkaline phosphatase activity showed a sudden drop. The glycogen, on the contrary, showed maximal deposition appearing in the epithelial cells, glandular lumen, and stroma, while blood vessels showed only traces. Glycoprotein was deposited in increasing amounts in the progestational phase; more of it was present in the glandular lumen than in the epithelial cells. The changes in endometrial glycogen found in this study coincided with those reported by others. The premenstrual peak was pronounced. Of 14 specimens obtained in the latter half of the menstrual cycle 6 showed proliferative activity and glycogen was present in varying amounts in these estrogen-stimulated endometriums. Glycogen was found in fairly large amounts in the stroma in the late progestational phase and variable amounts were seen in the late proliferative and early progestational stages.

On the whole the histochemical changes were predominant in the glandular and surface epithelium and rather slight in the stroma and blood vessels. A large amount of alkaline phosphatase was present in the proliferative phase, reached its peak in the early progestational phase, and dropped suddenly in the premenstrual phase. Although the amount of alkaline phosphatase in the glandular lumina was maximal in the early secretory phase, it was also maximal in the glandular and epithelial cells. The presence of alkaline phosphatase activity in the early progestational phase might be due to the influence of both estrogen and progesterone in this stage. Its disappearance in the late secretory phase might be due to a lack of estrogen.

The amount of alkaline phosphatase and glycogen in the late secretory phase showed an inverse ratio, which suggested formation of glycogen at the expense of phosphatase. Under the influence of estrogen, glycogen was synthesized in small amounts in the presence of large amounts of alkaline phosphatase. In the postovulatory phase both glycogen and alkaline phosphatase were present in large amounts, while progesterone might be involved in the activation of the catalytic reaction seen in the luteal phase. Further studies should help to clarify the problem of sterility.

Endometrium in Subfertility.—B. M. V. Shetty (*J. Obst. & Gynec. India*, vol. 10, December, 1959) reported the changes in glycogen and alkaline phosphatase in the endometriums of 102 unselected patients with subfertility. Of these 81 showed primary sterility, 11 relative sterility, and 10 habitual abortion. The specimens of endometrium were collected in the expected advanced secretory phase of the menstrual cycle. In three patients the endometrial tissue was insufficient and results were inconclusive. Of the remaining 99 specimens, 25 showed no evidence of ovulation, the endometrium being proliferative in 14 and hyperplastic in 11.

Over 80% of the patients showed good enzyme activity and low glycogen content, as is expected in a nonsecretory endometrium. Of 41 specimens with good glycogen content 7 showed poor alkaline phosphatase activity, and of 33 with low glycogen content 6 showed low enzyme distribution. The alkaline phosphatase activity was good in more than 80% of the specimens both in secretory and nonsecretory groups. No appreciable difference was seen among the secretory endometriums related to their glycogen content. All growing epithelial cells showed a good enzyme level. The presence of small quantities of glycogen in nonsecretory endometriums showed that this phenomenon by itself does not constitute evidence of ovulation. Of 74 specimens of secretory endometrium 44.6% showed deficiency of glycogen. Thus glycogen deficiency might be an important contributory factor in the causation of sterility and abortion.

UNITED KINGDOM

Promazine in Obstetrics.—MacVicar and Murray (*Brit. M. J.*, Feb. 27, 1960) give promazine to obstetric patients. The drug had no adverse effect on the course of labor, but its use, either alone or in combination with meperidine, caused amnesia in some patients and adequate sedation in most. Its use also lowered the total amount of analgesic and sedative required and thus benefited the mother and fetus. There was, however, an increase in the fetal heart rate. Promazine would seem to have a definite place in the treatment of the nervous primigravida early in labor.

College of General Practitioners.—Family physicians are appealing to the nation for contributions in the amount of $2.8 million to endow the College of General Practitioners, founded in 1952. Three main achievements of the college are that (1) more young doctors are entering general practice with knowledge and experience of what it entails, (2) more established doctors are keeping up to date through postgraduate study, and (3) medical research has been extended from the hospital and laboratory to the home.

So far the family physicians have maintained the college out of their own resources. Now its very success will jeopardize its future unless there is outside help. Medical advances in the past 25 years have increased family doctors' responsibilities and opportunities. The college was set up because of these responsibilities and to strengthen the contribution of general practice to the community. Foundation membership was restricted to physicians who met strict academic requirements or had 20 years of experience. There are now more than 4,900 members.

The money now sought will be spent for London headquarters, education of young doctors in diseases which seldom necessitate hospitalization of the patient, and a research foundation. Gifts and deeds of covenant should be sent to Coutts & Co., 440, Strand, London, W. C. 2.

Iron-Dextran Complex.—The *British Medical Journal* of March 12 called attention to the reported carcinogenic effect of iron-dextran complex, a preparation that has found a wide application in the treatment of iron-deficiency anemias, including those of pregnancy and rheumatoid arthritis. Although there must be general sympathy with any reputable pharmaceutical house which unexpectedly finds one of its products attended by possible hazards, both the public and the profession have the right to expect the highest standards of responsibility and caution. In all questions of carcinogenic hazard from environmental sources it is necessary to preserve a balance of judgment, but in the present case, though further work is desirable and is proceeding, the facts available are already more than sufficient to demand speedy withdrawal of the drug from any kind of general use in man.

Incidence of Diabetes.—During World War II an estimate was made of the number of diabetics in Britain who were then allowed an extra ration of fats, cheese, and butter. About 250,000 received these extra rations. This figure was also indicated by the sales of insulin and the assumption that only 50% of diabetics needed it. From this figure it was concluded that the incidence of diabetes in the population at large was 0.55%. Any such calculation today would be inaccurate as many diabetics are now treated with the oral hypoglycemic drugs. As the proportion of the population over 40 years of age is slowly increasing it is estimated that the number of diabetics in Britain may approach 500,000 (nearly 1% of the population within another decade or two).

Redhead (*Brit. M. J.* 1:695, 1960) conducted a survey of a large Newcastle general practice of 9,940 patients shared between four doctors. Nearly 2,000 patients selected at random had a urine test for glucose, and when glucose was found a glucose tolerance test or a two-hour postprandial blood sugar determination was done. As a result of the survey 19 cases of diabetes were detected, 9 of which were in known diabetics. Thus, over one-half the diabetics were discovered as a result of the survey. If this figure could be applied to the general population there must be about 250,000 undiagnosed diabetics in Great Britain and a total of nearly 500,000, or twice the number calculated 15 to 20 years ago. Most of the newly discovered cases in the Newcastle survey were in persons over 50 years of age. This confirms the view that as the human life span is prolonged, an increase in the number of diabetics must be expected.

Diagnosis of Lymphocytic Meningitis.—Tuberculous meningitis often starts as a lymphocytic meningitis, the bacterial cause of which may remain unknown until the results of culture or guinea-pig inoculation are available. In such cases antituberculosis therapy is often started, the diagnosis being made on suspicion and indirect laboratory evidence. This is justified in view of the risks run in delaying the treatment of tuberculous meningitis until the diagnosis is confirmed in the laboratory. On the other hand, injections of streptomycin may do harm if the patient does not have tuberculous meningitis but has acute poliomyelitis in the preparalytic stage. It is essential when dealing with a patient who has lymphocytic meningitis of undetermined cause to be able to exclude tuberculous meningitis. This can be done by examining the partition of a dose of bromide between the blood and spinal fluid. In normal subjects and in patients with nontuberculous lymphocytic meningitis the partition of bromide between blood and spinal fluid is about 3:1.

As the chemical analysis of small amounts of bromide is difficult and time-consuming, Crook and co-workers (*Brit. M. J.* 1:704, 1960) devised a technique for examining the partition of bromide. They used radioactive bromine (Br^{82}) which has a half life of 36 hours and emits β-rays of maximum energy 0.4 MeV, and γ-rays with energies in the range 0.55 to 1.47 MeV. A dose of 50 μc of sodium bromide containing Br^{82} was given orally in 50 ml. of water, and 48 hours later a lumbar puncture was done and the Br^{82} estimated by a scintillation counter. A simultaneous estimation was made in the blood serum. Diagnostic lumbar puncture on patients without meningitis gave opportunities for obtaining control data. With this technique the existence of a blood-spinal fluid barrier was confirmed in control patients without meningitis. In patients with lymphocytic meningitis the bromide distribution factor was not significantly altered, but in those with tuberculous meningitis it was lowered from the 3:1 ratio to less than 1:1. The advantages of this method are speed and simplicity.

Iproniazid and Angina.—Several investigators have claimed that iproniazid relieves anginal pain, although not all reports have been enthusiastic. Fife and co-workers (*Brit. M. J.* 1:692, 1960) made a controlled study of the drug in 51 patients with angina of effort. All patients gave a convincing history of cardiac pain on effort, and when dyspepsia was present roentgenograms were made to exclude gastric and gall bladder lesions. If these were present or if there was evidence of myocardial infarction within the previous six months or of anemia or other debilitating disease, the patient was excluded from the trial. In those selected, electrocardiograms were made after exercise sufficient to bring on chest pain or tightness. The severity of the condition was classified as mild, moderate, or severe according to the frequency of attacks and the ease with which they could be produced.

The trial was a double blind one, in which control tablets identical in appearance with those of iproniazid were used. The dosage was 50 mg. three times daily after meals for three weeks. The degree of improvement, if any, was recorded by the patients, who kept daily record cards. Iproniazid appeared to benefit 31 patients and the placebo 24, a difference that is not statistically significant. When the patients were asked to compare the effects of the two tablets, 14 thought that both were equally helpful and 13 that neither gave any relief. These figures are those that might be expected if both tablets were equally inert. Furthermore, 36 patients suffered from unpleasant side-effects such as dizziness, tiredness, weakness, palpitations, numbness of the limbs, difficulty in micturition, impotence, and dyspepsia when taking iproniazid. In view of the pronounced side-effects, including jaundice, and the marginal therapeutic response, it is doubtful if iproniazid should be used for the treatment of angina.

Monitoring the Artificial Kidney.—In order to reduce the personnel necessary to detect faults in the twin coil artificial kidney and to keep watch on the various instruments incorporated in it, Brennand and Bunker (*Lancet* 1:578, 1960) designed an electronic monitoring device which they call EMACK (electronic monitoring apparatus for coil kidney). Its functions are to measure the rate of blood flow through the kidney; to give audible and visual indication when the flow rate differs by more than ±10% from a previously selected rate; to indicate the temperature of the dialyzing fluid and control the tank temperature; to monitor the level of the dialyzing fluid and cut out the tank heaters automatically if the fluid volume falls below a safe level; and to indicate the pressure in the venous circuit. Its constructors claim that EMACK enables just two persons, a doctor and a nurse, to supervise the artificial kidney and the patient. Such defects as broken connections, kinked tubes, or a burst in the coil are signaled within a second or two, and any interference with the outflow from the kidney is signaled immediately. So far 60 dialyses have been done with the aid of EMACK.

CORRESPONDENCE

FREEDOM AND THE PHYSICIAN'S ROLE

To the Editor:—The controversy concerning so-called free systems of medical care versus socialized or government-sponsored plans is now several decades old. I do not propose to contribute here directly to this problem, by favoring one side or the other. I should like, rather, to call attention to some internal contradictions in the present state of American medicine. The immediate stimulus for these brief remarks, and my point of departure, is Hayek's book "The Constitution of Liberty" (Chicago, University of Chicago Press, 1960) and Kemp's recent comments on it in THE JOURNAL, Feb. 20, page 825.

Kemp used Hayek's book to underscore the dangers of the welfare state, especially in regard to governmentally or politically controlled systems of old age assistance and medical care. He quoted Hayek's warning that the so-called socialization of medicine threatens to transform doctors, "who have been members of a free profession primarily responsible to their patients, into paid servants of the state, officials who are necessarily subject to instruction by authority and who must be released from the duty of secrecy so far as authority is concerned" (p. 300).

I should like to comment briefly on the same problem as was discussed by Kemp, namely, the alternatives between two divergent types of medical care systems: the one "free," self-selective, and individualistic, the other "unfree," coercive, and collectivistic. In general, American medicine has favored the former and opposed the latter. Nevertheless, it has also permitted, perhaps even fostered, the operations of more or less coercive, nonprivate types of medical services under certain circumstances. As a result, there is a serious contradiction between the way in which medicine is actually practiced in the United States and the official positions of medical and psychiatric organizations. What exactly is this contradiction?

Consider the following situations, in each of which the physician functions as an agent of an organization, that is, as a "servant of the state," as Hayek and Kemp have stated: the military services, the Veterans Administration, the Public Health Service, medical schools, industrial organizations, labor unions, and the state mental hospitals. In none of these situations can there be an uncomplicated, direct, person-to-person relationship between patient and physician, a relationship of the type characteristic of "free" individualistic medical practice. Hence, physicians in the United States have few grounds on which to take a puristic stand in favor of individualistic systems of medical care. Some of these "unfree" (collectivistic) medical arrangements may be unavoidably tied to the development of complex socioeconomic conditions. I do not know how far this is the case, nor need this problem concern us here. What should concern us is the urgent need to recognize frankly the precise nature of our present state and, if necessary, to alter it so that it will conform more closely to our ideal image. I shall briefly illustrate the problem by taking psychiatric practice in state mental hospitals as an example.

The state hospital psychiatrist is, of course, a state employee. He is a servant of the state. This does not mean that he cannot be helpful to his patients, for the state usually defines his role so that it includes being a therapist for mentally sick patients. Significantly, however, such treasured medicoethical considerations as the patient's privacy and the confidentialness of communications between patient and doctor definitely do not obtain in this setting. The state hospital patient may be fingerprinted, his name may be kept on file in an office in the state capitol, and the record of his hospitalization may be made available to numerous agencies without his consent. In all these ways, the worst aspects of "state medicine," about which Hayek has warned, are with us right here and now.

The problem often cast as a conflict between "free" and "socialized" medicine is really a more general one; it is the problem of the ethical aims to which the practice of medicine may be put. If we wish to grapple with this problem, it is useful to ask the question: "Whose agent is the physician?" Clearly, as matters now stand, he may be the agent of a variety of different interests, the patient being but one of them. The possibility that the physician may serve primarily not the patient's but someone else's interests is most acute in psychiatric work. I have called attention (*Columbia Law Rev.* 58:183 [Feb.] 1958; *Am. Psychologist* 15:113 [Feb.] 1960; *A. M. A. Arch. Neurol. & Psychiat.* 76:432 [Oct.] 1956) to the fact that in different social situations different persons or parties hire, as it were, the psychiatrist. The old English proverb, "He who pays the piper may call the tune," comes to mind in this connection. Specifically, the psychiatrist may be an agent of any one of the following: the patient, the patient's relatives, schools, courts, military services, hospitals, and prisons. The psychiatrist's practical task will be determined in part by the nature of the interests he serves. His work will thus differ in accordance with these interests (*Psychiat. Quart.* 33:77 [Jan.] 1959).

I believe we would be in a better position to fight off further encroachments on "free" systems of medical care if, at the same time, we would remedy the defects in our existing system. Already we accept, as a matter of course, the fact that mental hospital patients should be treated as unfree persons. If we fail to correct this situation, which is perhaps only one instance of a larger trend, the similarities between penology and hospital psychiatry may extend and engulf all of medicine.

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CALORIC EQUIVALENTS OF GAINED OR LOST WEIGHT

To the Editor:—The article by Dr. W. L. Bloom entitled "Fasting as an Introduction to the Treatment of Obesity" (*Metabolism* 8:214 [May] 1959) which was summarized in The Journal, Jan. 23, page 328, prompts me to say that the subject of caloric equivalents of gained or lost weight under varying conditions has hardly been explored by workers in the field of metabolism. Knowledge of the following facts is essential. Carbohydrate and protein cannot be stored dry but retain with them three or more parts of water, while fat can be stored in an almost pure state. One gram of adipose tissue gives the body 8.3 calories of reserve energy, while retention of 1 Gm. of water-soaked glycogen or protein provides only about one calorie. These factors are basic for the determination of the caloric equivalents of gained or lost weight.

The average obese patient who is placed on a low-calorie diet for the purpose of weight reduction is practically in protein and carbohydrate equilibrium. The caloric deficit in these patients is made up almost entirely by the catabolism of fat. Under these circumstances 3,500 is the caloric value of one pound of body weight lost.

During fasting or when the diet is characterized by negative nitrogen and caloric balances, an entirely different situation obtains. This is strikingly demonstrated in Benedict's study of prolonged fasting (Benedict, F. G.: Study of Prolonged Fasting, Publication 203, Carnegie Institute of Washington, 1915, page 412). Benedict's subject fasted for 31 days, partaking only of distilled water. During this fast, 1.66 kg. (3.7 lb.) of protein, or 8.32 kg. (18.3 lb.) of flesh, were catabolized. Since the entire loss of body weight of this subject was 13.25 kg. (30 lb.), it can be seen that 63% of the total loss consisted of flesh catabolized. The amount of water lost concomitantly with the loss of flesh was enormous (6,383 ml., or 14 lb.). The amount lost concomitantly with the catabolism of fat was negligible (367 ml., or 0.8 lb.). The catabolism of 1.66 kg. of protein, which resulted in a loss of 8.32 kg. of body weight, yielded only 6,828 calories. If the fasting subject had been in protein and carbohydrate equilibrium, the 6,828 calories would have been derived from adipose tissue with a loss of only 0.83 kg. (1.8 lb.). The caloric equivalent of one pound of body weight lost by this fasting subject was 1,500. This is in striking contrast to the figure of 3,500 calories mentioned above in subjects who were in negative caloric balance but in nitrogen equilibrium.

It is necessary to stress the fundamental fact that, in fasting subjects or subjects who are in both negative caloric and negative nitrogen balance, a large part of the weight loss is not permanent. After the desired weight loss has occurred and the patient has been placed on a diet adequate to maintain caloric equilibrium, the protein stores which had been depleted during the period of negative nitrogen balance will be repleted. For every pound of protein (1,850 calories) deposited there will be an increase of 4 lb. (1.8 kg.) in body weight. Thus, even though the patient is in caloric equilibrium, he will continue to gain weight until the protein stores have been replenished. An expatiation of this subject may be found in the article "Caloric Equivalents of Gained or Lost Weight" by Wishnofsky (*Am. J. Clin. Nutrition* 6:542, 1958).

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LUNG CANCER IN DOGS

To the Editor:—Dr. Joseph Berkson's letter in The Journal, Feb. 27, 1960, page 967, prompts me to report a little item relating to the controversy over cigarette smoking in relation to lung cancer. I am reporting in narrative form, without specific documentation or figures.

In the summer of 1956, while in Moscow, I visited the Academy of Medical Sciences. There, at luncheon with Prof. V. N. Chernigovsky and Prof. V. V. Zakusov, I asked about the incidence of disease in Russia. They said that it was about the same as in the United States. I then asked about the incidence of lung cancer. Their reply was that an increase in the incidence of lung cancer in the large cities of Russia has been noted but no significant increase in the incidence of lung cancer in rural areas has occurred.

I then asked what was thought to be the cause of the increased incidence of lung cancer. The professors smiled good-naturedly and replied that it is not thought in Russia that cigarette smoking is the only cause of lung cancer. They indicated that it was thought that inhalation of any smoke might be a factor in promoting cancer. They pointed that there is a much lower consumption of cigarettes in Russia than in the United States and also that Russian cigarettes contain only a small amount of tobacco. But they also said that all the large Russian cities contain smog, as do large cities throughout the world. They told me that carcinogens have been isolated from the smog in Russian cities, as in Los Angeles, but that the smog is not caused by industrial pollution, since all the smokestacks in the Russian cities are equipped with Cottrell precipitators. Furthermore, they said, the smog is not due to automobiles since there are far fewer automobiles in Russian cities than in cities in the United States. They suggested that the smog might be due to exhausts from trucks. It does seem that there are many heavy buses and trucks in constant service in the major Russian cities.

Last year Dr. V. S. Rusinov of the Institute of Higher Nervous Activity of the Academy of Sciences of the USSR in Moscow visited the United States. He asked me if I recalled the discussion at the Academy of Medical Sciences on lung cancer in relation to tobacco smoking. When I replied in the affirmative, he went on to say that he had something interesting to report. What he had to say annoyed me, since I could not help but wonder why it was that someone in the United States had not thought of doing what he said was done in Russia. A survey was made of the incidence of lung cancer among dogs in the large cities and the incidence among dogs in rural areas, and the figures were compared. He said that there was significantly more lung cancer among dogs in large cities than in rural areas. This survey had been made by veterinarians. Such a survey has probably not been made in the United States because members of the medical profession do not often consult with those in veterinary medicine.

While no specific figures were reported and while the Russians are notoriously lacking in statistical sophistication, it nevertheless seems to me that these comments from Russian colleagues on their impressions on the relation between tobacco smoking and the incidence of lung cancer are worth recording.

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MEDICAL SOCIETY MEETINGS

To the Editor:—The editorial "Person to Person" in the Jan. 16 issue of The Journal prompts this letter. World War II and the simultaneous acceleration of laboratory discoveries in medicine marked a turning point in the character of medical society meetings in America. Before then, the theses presented were freely discussed by the audiences. There was a spirit, if not of equality between the speaker and audience, at least of the opportunity for equality. Since then, authoritarianism has been in the ascendant. The speaker is a teacher. Instead of the opportunity to discuss, the audience is given the opportunity to ask questions. Audience and speaker alike accept the difference in caste.

Although this change has not reached completion in all medical society meetings, the leaven is working in most. If the committees include papers other than medical college teachers' theses on the programs, it is often because the authors have the backing of research grants. The summary way in which they dismiss consideration of a thesis that is without the backing of an institution indicates that lack of such backing is held to be a sizable demerit. The contempt in which the authorities hold the product of their own teaching is an indication of a bad situation.

The void in medical knowledge is too great to permit research and its evaluation to be delegated to a select few or to permit the rank and file members of the profession to shirk their responsibility to observe and discuss. That physician would be dull indeed who could spend a lifetime in the practice of medicine without observing some previously unrecognized fact. Organized medicine should provide a forum of more easy access to the rank and file members in which their observations could be reported, further study encouraged or even aided, and the results made known.

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FREEDOM OF CHOICE

To the Editor:—The editorial "Freedom of Choice" in The Journal, Feb. 27, 1960, page 942, includes certain phrases which have been used vociferously by the medical profession for years. It is stated that "free choice of physician is the right of every individual" and that "such freedom of choice, together with free competition among physicians, constitute prerequisites to 'optimal medical care' ". There never has been and there never will be free choice of physician in the United States. Geography, economic status, limited numbers of physicians, and even race prohibit free choice. It cannot, therefore, be a prerequisite of optimal medical care.

Since "free choice of physician" does not exist, what does this phrase mean? It must mean that every person has a right to choose any doctor that he can reach, whose fee he can pay, whose personality suits him, and who will accept him. This point has nothing to do with optimal medical care, and the patient has no basis on which to judge the doctor's ability. The patient might be better off if a doctor were selected for him. "Free choice of physician" is intended to imply that the doctor is not an employee of a private or public organization and that his loyalty is totally to the patient. It is not divided between patient and employer as it would be if there were government control of medical services. The statement does not convey this meaning well.

The other confusing statement concerns free competition among physicians. About the only obvious competition is at an economic level and is not related to medical skills. Some of the poorest doctors have the largest practices. Most physicians make some effort to improve their professional excellence, but such efforts rarely create the furor that the economic struggles do. The editorial compares professional competition to the competition occurring in a market society, yet it was learned long ago that laissez-faire in the market place is unthinkable. Free competition among physicians is too wasteful. The people of the United States will not long be able to afford it. Since free competition, accurately defined, is not desirable, what is the term intended to imply? I am not sure. Competition among doctors can exist under government control of medicine, as it does in England. It can exist under private industrial control of medicine, as it does in Germany. To me the phrase is meaningless.

The two statements discussed have been used for so long by organized medicine that physicians no longer think about what they mean. They have become degraded to the tired level of a huckster's catchphrase. I believe they should be abandoned.

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PERIPHERAL NEUROPATHY

To the Editor:—The article "Peripheral Neuropathy After Exposure to an Ester of Dichlorophenoxyacetic Acid (2,4-D)" in The Journal, Nov. 7, 1959, page 1306, reports three cases allegedly caused by skin absorption of this compound. The authors point out that the time relationships in all three patients were such that the herbicide could reasonably be implicated. Since these cases appear to be the first of their kind to be reported, it is unfortunate that incomplete information was given concerning the nature of the 2,4-D preparation used by these patients.

In toxicology it is well known that such things as vehicles, solvents, and emulsifiers may have significant toxic actions of their own. Not infrequently they may be more dangerous than the specific active ingredient in a compound. A familiar example is the use of carbon tetrachloride as a solvent for DDT in the early days of World War II, which resulted in a number of cases of carbon tetrachloride poisoning.

Recent developments in the use of pesticides call for dissemination among physicians of information about the possible harmful effects of careless and indiscriminate use of these materials. It is equally important that accurate chemical and clinical data be provided so that correct diagnoses can be made and proper etiologies determined. While the cases in question may actually have been due to 2,4-D, the possibility has not been excluded that other agents, alone or in combination, may have been responsible. Complete chemical data would have added greatly to the value of this report. In their absence the authors might at least have mentioned the possibility of other chemicals being involved.

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New York 32.

The above comment was referred to the authors of the article cited, and they have submitted the following reply.

To the Editor:—Doctor Goldwater's points are well taken. The vehicle must be taken into account, and in the usual commercial preparation of the esters of 2,4-D the vehicle is usually a petroleum solvent plus an emulsifier, but these are usually listed as inert ingredients by the manufacturer. Dr. R. B. Hurl of Marysville, Ohio, wrote to us and raised the question about the possible role of the petroleum solvent and the emulsifier in the causation of the peripheral neuropathy. Dr. Hurl suggested that "perhaps it is safer to say that certain proprietary ester formulations of 2,4-D have caused peripheral neuropathy." We agree with this point of view, since the essential point of our article was that undue exposure to a commercial preparation of an ester of 2,4-D was followed by peripheral neuropathy. In one instance we were able to obtain the label from the container of the 2,4-D preparation. On the label, the manufacturer stated that the preparation contained "2,4-dichlorophenoxyacetic acid, isopropyl ester 44%" and "inert ingredients 56%."

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TREATMENT OF MICROBIAL FOOD POISONING

To the Editor:—I trust Dr. G. M. Dack will allow me to criticize one portion of his excellent article, "Current Status of Therapy in Microbial Food Poisoning," published in The Journal, Feb. 27, page 929. I believe that his description of the treatment of patients with botulism leaves something to be desired. I have the feeling, perhaps unjustified, that when describing his management of secretions and failing respiration in the unhappy patients with this disease, he is writing more from the viewpoint of the general behind the lines than from the actual battle field.

For example, tracheostomy is not even mentioned, and it is urgently necessary in these patients not only to clear secretions and secure a patent airway but also to protect against fatal pulmonary aspiration of stomach contents. His admonition that oral feeding should be avoided is worth heeding; in fact, one should go a step further and periodically empty the stomach of gastric secretions, as dilatation is a common condition in such patients.

The statement that "there is no agreement among clinicians regarding the value of respirators in the treatment of botulism" is astonishing, particularly in the light of the immediately preceding sentence, in which it is stated that "artificial respiration may be required." Just how Dr. Dack proposes to maintain the prolonged artificial respiration required in these cases without a mechanical ventilator escapes me. It seems virtually certain that the only hope for survival of patients whose respiratory function is severely involved in this disease lies in the early and competent application of modern respirator care.

Dr. Dack unwittingly falls into an error of omission when he states that "the patient should be kept in quiet, restful surroundings and encouraged to avoid unnecessary muscular exertion." This statement is all right as far as it goes, but it has the potential of lulling the unwary into an apathetic condition from which he arises too late and finds his patient dead from asphyxia. It is reminiscent of the type of wishful thinking which once prevailed about the management of bulbospinal paralysis in patients with poliomyelitis. In retrospect, it is disheartening to consider the number of such patients who died without being afforded the benefits of proper airway and respirator care because such vigorous ministrations ran counter to the dogma of rest and quiet. Laudable though they may be in theory, rest and quiet and avoidance of unnecessary muscular exertion never resuscitated an unfortunate victim of respiratory paralysis. Hypoventilation and asphyxia, be it insidiously chronic or dramatically acute and from whatever cause, must be dealt with vigorously and efficiently. Properly applied, tracheostomy and artificial ventilation by mechanical means can be lifesaving and should constitute an important part of the treatment of prolonged bulbar and respiratory paralysis from all causes. The recent report of a case of botulinus poisoning by Southerland (*J. A. M. A.* 172:1266 [March 19] 1960) is a case in point. The respirator undoubtedly saved this patient's life. One wonders why tracheotomy was not performed here, however, for it was an obvious logical step in the face of the inability to cope with secretions and probably would have prevented the pneumonia which developed.

These remarks are intended as constructive criticism of the one obviously weak portion of an otherwise excellent discussion. There seems little point in expending a great deal of effort on all other aspects of botulism, only to allow the patient to die of respiratory insufficiency.

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THE GETTLER TEST FOR DROWNING

To the Editor:—Russell S. Fisher, M.D., in his article, "Recent Developments in Forensic Pathology," in The Journal, Feb. 27, page 896, states that "the Gettler test for drowning was described nearly two decades ago." In July, 1929, I spent a week with Doctor Gonzales in the office of the Medical Examiner in New York, and Gettler's test was discussed with me at that time, nearly 31 years ago.

Doctor Fisher states that the Gettler test "depends on the assumption that, in persons drowning in sea water, the ingestion of highly saline water will lead to an increased blood chloride concentration in the left heart as compared to the right and, in persons drowning in fresh water, a dilution of blood chlorides in the left heart as compared to the right." In some way Doctor Fisher has substituted the word "ingestion" for "inhalation." It is impossible for materials ingested to reach the left side of the heart without first passing through the right side of the heart.

Gettler's test was based on the assumption that, in persons drowning in sea water, the inhalation of highly saline water would lead to a higher chloride content in the blood in the left side of the heart than in the right side. Salt water taken into the lungs, not into the stomach, would give up some of its chloride to blood passing through the lungs from the right side of the heart to the left side. Hence there would be a higher chloride content in the left than in the right side.

Fisher makes the same error in writing of the test described by Durlacher and others by again referring to "ingestion of water." He quite properly mentions certain limitations to the Gettler test. There is another limitation which I do not recall having seen in the literature. It is not rare for one drowning in sea water to have severe laryngospasm as a result of the intense irritation caused by the first salt water which enters and to die of suffocation with so little sea water in the lungs that no significant difference in chloride content of the blood in the two sides of the heart results. Under such circumstances neither the Gettler test nor the Durlacher test would be valid.

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MEDICAL LITERATURE ABSTRACTS

INTERNAL MEDICINE

Aseptic Meningitis Syndrome: Report of 11 Cases with Cerebrospinal Fluid Isolation of Enteroviruses. S. Saslaw, C. F. Wooley, and G. R. Anderson. A. M. A. Arch. Int. Med. 105:69-75 (Jan.) 1960 [Chicago].

Association between enteroviruses and the aseptic meningitis syndrome was demonstrated by recovery of specific virus strains directly from the cerebrospinal fluid. It is the purpose of this study to describe the clinical and laboratory findings in 11 adult patients with aseptic meningitis having the equine encephalitis, mumps, lympho-Coxsackie, or enteric cytopathogenic human orphan (ECHO) viruses. ECHO virus, type 9, was recovered from 5 patients; Coxsackie virus, group A, type 9, from 3 patients; and Coxsackie virus, group B, type 4, from 1 patient, and type 5, from 2 patients. From 4 of these 11 patients an identical isolate (2 Coxsackie A9, 1 Coxsackie B4, and 1 Coxsackie B5) was obtained from the feces. The occurrence of the syndrome was mainly seasonal. Definite localized muscle weakness was present in one patient. Three of the 6 women at the time of admission were in the 1st or the 2nd trimester of otherwise uneventful pregnancies. The cerebrospinal fluid changes were not diagnostic per se; however, they were consistent with established fluid changes in viral disease of the central nervous system. This study serves to illustrate the diverse etiology of the aseptic meningitis syndrome.

The Normal Systolic Murmur. D. Groom, W. Chapman, W. W. Francis, and others. Ann. Int. Med. 52:134-144 (Jan.) 1960 [Lancaster, Pa.].

The terms "physiological," "functional," "innocent," and "benign" have customarily been applied to heart murmurs which, by definition, arise in presumably normal hearts. It has been variously estimated that from about 5 to 15% of normal subjects have functional heart murmurs which are audible on stethoscopic examination. The authors were particularly interested in functional systolic murmurs that may be recorded from the precordium of virtually all normal subjects at rest. There are 2 requisites: a nonacoustical type of pickup for electronic reproduction of sounds and a soundproof room. Recordings were made on a cathode-ray oscilloscope from 71 normal adult subjects. In none of them was a murmur audible on ordinary stethoscopic examination. Recordings were made with the subject at rest in the supine position.

All the subjects showed murmurs, extending through one-fourth or more of systole, and reproducible on repeated tracings. In more than three-fourths of them, the point of maximal intensity was between the 2nd and the 4th intercostal space along the left sternal border. Wave forms of most murmurs showed some sinusoidal characteristics, with fundamental frequencies of 60 to 90 cps, and secondary frequencies an octave or more higher. The majority of the murmurs were of decrescendo configuration after the 1st heart sound. Their intensity tended to vary from day to day, with different phases of respiration or changes in position, and with exercise. Short diastolic sounds were recognizable in the tracings of a few of the subjects.

With the same technique, murmurs were found in 19 of 25 fetal hearts recorded during the last trimester of gestation. Presumably the fetal murmurs are systolic in time, and arise from shunts unique to the fetal circulation. The mechanism and site of origin of these systolic sounds in the adult are uncertain. However, their presence is understandable on the basis of what is known of circulatory dynamics, and it appears that they represent a universal functional murmur which is usually subaudible.

Pruritus: A Neglected Symptom in Thyrotoxicosis. M. Eliakim and M. Rachmilewitz. Israel M. J. 18: 262-268 (Nov.-Dec.) 1959 (In English) [Jerusalem].

Severe pruritus was one of the symptoms in 6 patients with thyrotoxicosis. The itching was generalized, migrating, unpredictable, and often more pronounced at night. No skin lesions were observed, except for dermographia. Scratching afforded no relief. In all instances, itching was one of the first signs to disappear with successful treatment. Ergotamine and tetraethylammonium chloride afforded temporary symptomatic relief of pruritus in 2 patients. All the patients received propylthiouracil.

The place of publication of the periodical appears in brackets preceding each abstract.

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In addition, 3 patients received Lugol's solution and underwent subtotal thyroidectomy. Radioiodine (I^{131}) was given to one patient. Itching usually disappeared from 7 to 10 days after treatment with propylthiouracil began, even before other signs of improvement were noted. Cutaneous vasodilatation and marked instability of the autonomic nervous system are considered the pathogenic factors of pruritus in thyrotoxicosis.

Pleurisy and Pericarditis Complicating Myocardial Infarction: The So-Called Postmyocardial Infarction Syndrome. G. Cohen, I. Dardick and J. Greenblatt. Canad. M. A. J. 82:123-130 (Jan. 16) 1960 [Toronto].

The cases of 10 patients (2 women and 8 men), who ranged in age from 48 to 80 years and who had a syndrome resembling idiopathic pericarditis complicating myocardial infarction, are presented. This unique clinical picture, which occurs at varying intervals after an acute attack of coronary thrombosis, has been seen sporadically in the past but was first systematically described by Dressler. Most of the patients in this series were seen in the summer of 1958, and infection, probably viral, is suggested as the most likely cause of their syndrome. The possible relationships to idiopathic pericarditis, pleurodynia, and the postcommissurotomy syndrome are discussed.

Effect of Pretreatment with Methylthiouracil on Results of ^{131}I Therapy. J. Crooks, W. W. Buchanan, E. J. Wayne and E. MacDonald. Brit. M. J. 1:151-154 (Jan. 16) 1960 [London].

It might be expected that thyroid tissue would become more sensitive to ionizing radiations after treatment with antithyroid drugs which increase both the vascularity of the gland and the number of mitoses in thyroid cells. Indeed, some investigators had gained the impression that patients who had been pretreated with methylthiouracil required a lower dose of radioiodine (I^{131}) than untreated patients. Since I^{131} produces its effects relatively slowly, it may be necessary to control thyrotoxicosis with antithyroid drugs before treatment with the radioisotope. Furthermore, many patients who are treated with I^{131} have previously received courses of antithyroid drugs. To ascertain whether pretreatment with methylthiouracil influenced the results of I^{131} therapy, the authors made studies on 4 groups of patients.

Group 1 consisted of 28 patients who had been treated with methylthiouracil for from 3 months to 1 year, and who were either euthyroid or had a minor degree of thyrotoxicosis when the I^{131} treatment was given one week after the administration of methylthiouracil was stopped. The 45 patients of group 2 were treated with I^{131} in the same manner as those of group 1, but they had never received an antithyroid drug. Group 3 consisted of 21 patients who had previously been treated with methylthiouracil in the same way as those in group 1 but in whom the dose of I^{131}, estimated in the standard manner, was arbitrarily increased by 25%. Group 4 acted as a control to group 3; it included 56 patients who were not pretreated and whose dose was determined in the same way as that of patients in groups 1 and 2; group 4 differed from group 2 only in that the patients were treated contemporaneously with group 3.

In order to determine the 48-hour gland take-up of I^{131}, most patients were given a tracer dose during the week before treatment with the radioisotope. It was decided that patients with impalpable glands would be given doses of 4 or 5 mc., and those with minimal but definite diffuse enlargement of the gland doses of 6 or 7 mc.; patients with larger glands received from 7 to 25 mc. according to the size of the goiter. Other factors besides gland size influenced the dose prescribed; for example, patients who had undergone thyroidectomy were given 5 or 6 mc., unless the gland remnant was exceptionally large. Relatively high doses were given to patients with nodular glands, cardiac failure, and uncontrolled diabetes mellitus, or whenever the risk of producing hypothyroidism was less than the need for a rapid remission of symptoms. The patients were observed at monthly intervals until they had become euthyroid. The assessment was initially made on clinical grounds but was confirmed by a basal metabolic rate estimation. The necessity for retreatment was based on the same principles as those for the first treatment. Patients whose cases were doubtful were observed for 2 more months, before they were readmitted to hospital for further study.

I^{131} therapy in patients pretreated with methylthiouracil (group 1) showed a significantly lower one-dose cure rate than it did in patients who had received no pretreatment (group 2). This finding could not be accounted for by variations in gland types between the 2 groups. Increasing the dose of I^{131} in pretreated cases (group 3) raised the one-dose cure rate to that of an untreated control group (group 4). The authors conclude that methylthiouracil makes the thyroid relatively radioresistant.

Cardiovascular Study of 100 Asthmatic Patients with Special Reference to Electrocardiographic Changes. O. A. Robiolo, P. R. Tuero and L. Bentolila. An. cir. 24:151-156 (July-Sept.) 1959 (In Spanish) [Rosario, Argentina].

Asthma of long duration has frequently been incriminated as a cause of heart disease. One hundred patients of either sex with asthma of long duration were observed. Most of the patients were between the ages of 40 and 70 years, and complained of either cardiovascular or respiratory disorders. Twenty patients had pulmonary emphysema. The electrocardiograms showed changes of either atrial or ventricular overload in 16 of these patients; in the remaining 4 the electrocardiograms were normal. Forty-four patients had arterial hypertension; 9, coronary insufficiency; and 4, chronic cor pulmonale which was associated with pulmonary emphysema. Roentgenologic examination of the heart showed changes proper of overload of the lesser circulation in 7 patients, whereas the electrocardiograms showed this type of changes in 37 patients. Overload of the lesser circulation showed early in the electrocardiograms by changes of the P wave, associated with elongation of the PQ interval by about 0.20 second. The sinusal rhythm was regular. The cardiovascular disorders, as shown by changes of the electrocardiograms observed in patients with asthma of long duration, depend on the presence of pulmonary hypertension which results from secondary emphysema.

Takayasu's Syndrome and Ischemic Ophthalmopathy: Study of a Typical Case. J. Barraquer, J. Escribano and P. González-Marin. Med. clin. 33:171-178 (Sept.) 1959 (In Spanish) [Barcelona, Spain].

A typical case of aortic arch syndrome (Takayasu's disease) is reported. The patient, a 40-year-old woman, had felt the first symptoms at the age of 35, with the onset of severe headaches 3 or 4 months after the birth of her youngest child. She had a burning sensation in the frontal area and numbing of the parietotemporal regions. Paresthesia in the fingers of both hands, claudication in the left hand and leg, and visual disorders occurred in succession. Loss of weight and of mental alertness, as well as weakness in both arms, ensued. The patient's hair became thin and dry. Bilateral absence of radial pulse was noted. Under a combined prednisone-penicillin therapy, the patient improved and recovered some strength in her arms and left leg. Visual disorders occurred, with loss of sight in the left eye. The atrophy of facial teguments and the loss of teeth, because of pyorrhea, gave the patient the appearance of a much older woman. Intumescent cataracts were present in both eyes, and the orbits were excavated. The tongue became reduced in size and acquired the aspect of a bird's tongue. Neither the radial nor the carotid pulse could be felt.

The patient was treated with 20 mg. of prednisone daily and with liver extract, to which injections of benzathine penicillin were added. Six months later there was considerable improvement in the clinical picture; the headaches had subsided, and the patient had gained weight. The cataract in the left eye was extracted, and the postoperative period was satisfactory, although the headaches recurred. Only a slight visual improvement was obtained, however. The administration of prednisone and ethyl biscoumacetate brought about some relief of the headaches, and the patient was discharged from the hospital. The prognosis was that of a progressive arteritis-thrombosing process.

Ventricular Fibrillation: Treatment and Prevention by Electric Currents. P. M. Zoll, A. J. Linenthal and L. R. N. Zarsky. New England J. Med. 262:105-112 (Jan. 21) 1960 [Boston].

Additional experiences in the use of external countershock and external electric stimulation in terminating and preventing ventricular tachycardia and fibrillation are presented by the authors, confirming the clinical value of such treatment as reported in previous articles, abstracts of which were published in The Journal (161:1102 [July 14] 1956 and 163:311-312 [Jan. 26] 1957). Ventricular tachycardia or fibrillation was terminated 532 times in 8 new patients. Five of these had cerebral syncope with bradycardia (Stokes-Adams disease), one had atrial fibrillation treated with digitalis, one had multifocal premature beats treated with quinidine, and one had normal sinus rhythm. Alternating current (60 cycle, 0.15 second, 150 to 450 volts) was applied to the unopened chest with large electrodes. The countershock was applied as soon as possible after the onset of the arrhythmia, always after a sufficient interval (usually more than 15 seconds), so that the patient was unconscious and did not experience pain. An initial shock with 150 to 250 volts was usually applied; if ineffective, successively larger ones were given every few seconds. Seldom were more than 450 volts necessary. During the application of the high-voltage currents, precautions were taken that each electrode handle was held by a different person and that no one touched the electrodes or the patient.

The technique is immediately effective, clinically feasible, and safe. The major limitation of successful resuscitation is delay in its use. Successful defibrillation depends on immediate recognition of the emergency, immediate identification of the arrhythmia, and prompt application of external countershock, all within 4 minutes, before the heart and the brain suffer damage. This limitation can be met by cardiac monitoring, which provides immediate recognition of cardiac arrest and identification of the arrhythmia. The principal remaining problem is the prevention of recurrent seizures. Quinidine, procaine amide, and potassium salts, which depress cardiac rhythmicity and irritability and are ordinarily useful in the treatment and prevention of ventricular arrhythmias, are contraindicated in patients with complete heart block. External electric cardiac stimulation at the rates above the basic idioventricular rate has been effective in preventing these recurrent ventricular arrhythmias. In the 8 patients reported in this article, the technique was applied continuously for periods as long as 4 days. As the patient may develop pain and skin ulcerations, at times the stimulation has to be interrupted.

Retinopathy and Nephropathy in Diabetes Mellitus: Comparison of the Effects of Two Forms of Treatment. S. Johnsson. Diabetes 9:1-8 (Jan.-Feb.) 1960 [New York].

The occurrence of nephropathy and retinopathy was studied in 2 series of diabetic patients in Malmö, Sweden. Series 1 comprised all surviving patients (54) whose diabetes mellitus had been discovered between 1922 and 1935; series 2 comprised all surviving patients (105) whose disease had been discovered between 1936 and 1945 and who were under 40 years of age. Nineteen of the patients in series 1 and 5 in series 2 had died of late diabetic complications. All the patients, except one, were seen personally by the author. Those in series 1 had been on a strictly regulated diet for four-fifths of the duration of their diabetes and had received 2 or 3 injections of short-acting insulin a day. Those in series 2 had been allowed a free diet during 85% of the total course of their disease and had received one injection daily of long-acting insulin.

The frequency of nephropathy was significantly lower in series 1, in spite of the longer duration of the condition. Although no significant difference was found in the frequency of retinopathy between the 2 series, severe retinopathy with impairment of vision was more common in series 2. Eight patients in series 1 had had insulin coma on more than 20 occasions; they were all free from proteinuria after 25 years of diabetes, which suggests that frequent insulin coma does not favor the occurrence of nephropathy or retinopathy. The results support the increasingly common opinion that good control of diabetes delays the development of late diabetic manifestations. As long as the etiological factor in these complications remains unknown, it is advisable to control the carbohydrate metabolism as carefully as possible. A well-controlled diabetes, with 2 daily injections of insulin, is preferable to the not so well-controlled condition which is the rule when only one daily injection is given.

Familial Nonhemolytic Jaundice with Normal Liver Histology and Conjugated Bilirubin. B. J. Haverback and S. K. Wirtschafter. New England J. Med. 262:113-117 (Jan. 21) 1960 [Boston].

A syndrome of familial nonhemolytic jaundice, with elevated serum levels of conjugated and unconjugated bilirubin, is described. Jaundice starts at an early age, and, unlike the findings in the congenital form of hemolytic jaundice (Gilbert's disease), conjugated bilirubin is present in both serum and bile. Three cases of this syndrome, occurring in the same family, are reported. A 27-year-old man and his 32-year-old sister had had jaundice for the first time at the ages of 4 and 1 respectively. Both brother and sister had dark urine with large amounts of bilirubin, as well as elevated direct and indirect serum bilirubin values. Both patients had had occasional episodes of abdominal pain and fatigue. In the woman, jaundice decreased during each pregnancy and increased again after delivery. The patients seemed to be in general good health except for the jaundice. A liver biopsy in the first patient and physical examination of his sister revealed no liver abnormality. The patients' father had been jaundiced for many years, and the mother was thought to have had occasional episodes of clinical jaundice. Three other members of the family, who lived abroad, were reported to have had clinical jaundice for prolonged periods.

It is likely that the family described by the authors represents the syndrome of familial nonhemolytic jaundice described by Rotor and his associates. The clinical characteristics of this syndrome resemble features of both Gilbert's disease and chronic idiopathic jaundice, although chemical and histological findings clearly separate the 3 entities. The question is raised as to whether the nature of the defective function in this syndrome is different from that in chronic idiopathic jaundice. If the defects are different in the 2 diseases, it is possible that more than one system is involved in the excretion of bilirubin conjugates.

Treatment of Diabetes with Metahexamide. R. H. Pollen, R. H. Barnes, D. C. Tanner and others. Diabetes 9:25-30 (Jan.-Feb.) 1960 [New York].

The effects of metahexamide were studied in 92 diabetic patients for periods which varied from a few days to 8 months. Twenty-five patients had already had an unsatisfactory response to another sulfonylurea compound, and 18 had had a diagnosis of diabetes mellitus made before the age of 40. Most patients were older persons with mild diabetes, selected on the basis of their known responsiveness to sulfonylurea compounds. Insulin was withdrawn abruptly from the patients who required less than 40 units daily, and its dosage was reduced in those who had a more labile disorder or who required more than 40 units daily. Metahexamide was given in an initial dose of 200 mg. daily during the first 3 or 4 days. The dosage was then reduced to from 50 to 200 mg. The maintenance dose was 100 mg. once a day for most patients. The results were evaluated as good control when the blood glucose value was below 130 mg. per 100 cc. in fasting, or below 150 mg. 2 hours postprandially, and a urine specimen obtained before meals contained no glucose or only a trace. Fair control meant that the blood glucose level was below 150 mg. per 100 cc. in fasting, or below 180 mg. 2 hours postprandially.

Good control was obtained in 39 patients (42.5%), and fair control, in 10 (10.9%). In 43 patients (46.6%) there was no response to the therapy. The authors believe that, although the efficacy of metahexamide compares favorably with that of tolbutamide or chlorpropamide, the larger number of instances of hepatotoxicity and jaundice, which have been reported with metahexamide as compared with chlorpropamide, suggest that the toxicity of metahexamide precludes its usefulness as a therapeutic agent. In this series the side-effects included malaise in 2 patients, gastrointestinal symptoms in one, prolonged prothrombin time in one, and hepatic dysfunction in one. These 5 patients had to be withdrawn from the treatment.

SURGERY

Acute Extradural Hematomas Without Demonstrable Skull Fractures. J. Mealey Jr. J. Neurosurg. 17:27-34 (Jan.) 1960 [Chicago].

The author reports on 34 patients with traumatic extradural hemorrhage, predominantly of the middle fossa, who have been treated by craniectomy or osteoplastic craniotomy, with evacuation of the compressive clot, since 1935 at the Massachusetts General Hospital in Boston. The ages of the patients ranged from less than 5 up to 65 years. Six of them were children, between the ages of 11 and 15 years. Five of the children proved to have large extradural hemorrhages without associated fractures, as revealed by roentgenograms of the skull or by surgical exploration. The hemorrhages were acute in nature and occurred after relatively minor injuries, without well-documented unconsciousness immediately after the trauma. The latent period varied from 1 to 4 hours in 4 patients, and was about 23 hours in the 5th. Prominent symptoms during this time were severe headaches and lethargy. Major findings at the diagnostic examinations in the first 3 patients included deep coma and/or decerebrate posture with ipsilateral dilated, fixed pupils. In the remaining 2 patients deep stupor and hemiparesis without anisocoria or pupillary fixation to light were found. These findings developed within 12 hours of the time when, by history, the 5 patients were no longer conscious.

The time from injury to operation varied from 5 to 28 hours. There was no precise correlation between the source of hemorrhage found at operation and the clinical course. Four of the hemorrhages were believed to be arterial in origin, either from the middle meningeal arterial trunk or from its major subdivisions; the sources of hemorrhage were multiple venous in one patient. One of the 5 children with acute extradural hemorrhage without fracture died, a mortality rate of 20%. Of the surviving children, 3 were normal and 1 had a neurological deficit at discharge from hospital. The incidence of acute extradural hematoma without associated skull fracture is significant, and is considerably greater in children than in adults.

Treatment of Advanced Carcinoma of the Breast by Bilateral Oophorectomy and Prednisone. D. M. Brinkley and E. K. Pillers. Lancet 1:123-126 (Jan. 16) 1960 [London].

Eighty-two patients with advanced carcinoma of the breast were subjected to bilateral oophorectomy and to prednisone treatment. "Hormone therapy" had been prescribed to 42 patients of this series, and oophorectomy was undertaken when remissions from this treatment had been exhausted. Of the 82 patients, 66 had failed to respond satisfactorily to previous radical surgery and radiotherapy; 24 of them, however, had a satisfactory response, with definite objective improvement, after oophorectomy and prednisone treatment, and prolongation of useful life expectancy was obtained, averaging 16½ months as compared with 6 months for the other 42 patients. Of the 82 patients, 16 had had no previous treatment and were initially subjected to oophorectomy and prednisone treatment; 9 of these had a satisfactory response, with an average survival time of 16 months as compared with 3 months for the other 7 patients. The menopausal status, the presence of metastases to the ovaries or to the liver, and the duration of the disease before oophorectomy appeared to be of no definite prognostic significance.

The authors believe that treatment with prednisone at doses of 10 mg. twice a day should be started as soon as possible—generally within 48 to 72 hours—after oophorectomy. From their experience with the present series, they conclude that patients who have had a remission after androgen treatment are likely to get a further remission from oophorectomy and prednisone therapy. Failure to respond to androgen treatment does not necessarily imply that oophorectomy will fail. The authors consider bilateral oophorectomy and the administration of prednisone a useful treatment of patients with advanced carcinoma of the breast.

Subtotal Gastrectomy for Bleeding Duodenal Ulcer in Childhood: Report of Three Cases, with Six-Year Follow-up in One. T. H. Green and W. H. Hendren. New England J. Med. 262:118-122 (Jan. 21) 1960 [Boston].

The authors report on 2 cases of chronic duodenal ulcer and 1 case of duodenitis in children with recurrent massive bleeding and chronic obstruction, which had failed to respond to medical therapy and which were eventually treated by subtotal gastrectomy. The first patient, a 12-year-old boy with a diagnosis of peptic ulcer established by roentgenography, was first treated clinically. He was discharged in good condition after a 28-day stay in the hospital, but 15 months later, after a period in which he disregarded all dietary prescriptions, he was again hospitalized, with continuing hemorrhage, a pulse of 120, and a hemoglobin level of 6.5 Gm. per 100 cc. After several blood transfusions, a subtotal gastrectomy was performed, followed by a retrocolic Hofmeister gastroenterostomy. Five years after the operation, in spite of his dietary habits and excessive smoking, the patient physically was a well-developed youth. An episode of bleeding, which occurred 6 months later, was treated by a transthoracic vagotomy.

The second patient, a 10-year-old boy with a duodenal ulcer demonstrated by x-ray study, underwent a subtotal gastrectomy and a retrocolic Hofmeister gastroenterostomy after being treated clinically on 2 different occasions. The postoperative period was uneventful. Nine months after the operation the patient was well, with a normal diet and appetite, satisfactory growth, and maintenance of weight. The third patient, a 6-year-old boy, was hospitalized because of a massive gastric hemorrhage. A program of fresh-blood replacement and ulcer diet was instituted, but as the patient continued to bleed, a longitudinal gastrectomy was performed. The blood was found to be welling from the duodenum, which was diffusely reddened, although no definite ulcer could be identified. The proximal portion of the duodenum was resected, and the continuity of the intestinal tract was reestablished with a retrocolic Pólya anastomosis. Examination of the specimen revealed only focal necrosis and submucosal hemorrhage of the duodenum. Fifteen months after the gastric resection the patient was on a normal diet, was well nourished, and was growing normally.

These experiences and similar reports indicate that children may have acute and chronic ulcers entirely similar in behavior and need for surgical therapy to those seen in adults. The surgical procedure deals adequately with the ulcer and its complications without interfering with the subsequent physical growth of the child.

The Dumping Syndrome: I. Factors Responsible for the Symptoms. L. P. Le Quesne, M. Hobsley and B. H. Hand. Brit. M. J. 1:141-147 (Jan. 16) 1960 [London].

It had been suggested that, in the absence of the pylorus, the unduly rapid passage of hyperosmotic food and its derivatives into the small intestine causes a shift of fluid from the vascular compartment with a fall in circulating volume, and this, in turn, causes the dumping symptoms. The authors feel that, if this were true, it would be difficult to understand why all patients do not experience dumping symptoms after partial gastrectomy. To clarify the role of a fall in plasma volume in the production of dumping symptoms, they not only investigated the effect of hypertonic glucose in the production of symptoms and a fall in plasma volume, but also observed the patient's response to a reduction in circulating volume produced by the application of thigh cuffs. These investigations were carried out in 2 groups of patients: (1) 16 patients upon whom the test was performed before and at intervals after partial gastrectomy, and (2) 11 patients with the dumping syndrome. In some of these patients additional tests were performed.

In all but one of the patients who at the time of testing were experiencing postcibal dumping symptoms, the oral administration of hypertonic glucose reproduced these symptoms; the glucose never produced symptoms in those who were symptom-free after meals. The hypertonic glucose produced a fall in plasma volume, which was significantly greater in those with than in those without symptoms, but there was a definite overlap between the 2 groups. The results of the thigh-cuffing observations showed that this overlap was due to differences in the individual response to a sudden fall in circulating volume. Additional evidence linking the systemic symptoms of the dumping syndrome with the fall in plasma volume was provided by replacement infusion experiments, by observations on 2 patients who spontaneously recovered from the syndrome, and by observations on a patient before and after closure of a gastroenterostomy.

It is concluded that the dumping syndrome is due to the passage of hyperosmotic solutions into the upper intestine, causing in some patients a rapid transfer of fluid from the vascular compartment into the intestine. This results in intestinal distention and an abrupt fall in circulating volume, which, in subjects intolerant of such a fall, gives rise to the systemic symptoms.

The Dumping Syndrome: II. Cause of the Syndrome and the Rationale of Its Treatment. M. Hobsley. Brit. M. J. 1:147-151 (Jan. 16) 1960 [London].

In the studies presented in this paper, the author has examined the relation of changes in the blood sugar concentration to changes in the plasma volume. Observations were made on (1) changes in blood sugar concentration and (2) changes in plasma volume after the oral administration of 175 ml. of 50% glucose solution to 26 patients who had undergone gastrectomy and to 1 patient who had had a gastroenterostomy.

In patients with a large fall in plasma volume after the ingestion of hypertonic glucose, the rise in blood sugar value was more pronounced and prolonged than in those with a small fall. A direct linear correlation was found between the maximum fall in plasma volume caused by the hypertonic glucose and the rate at which the blood sugar concentration rose in the first 10 minutes after the ingestion of glucose. In patients in whom the hypertonic glucose caused a large fall (more than 8%) in plasma volume, the administration of insulin, so as to lower the blood sugar concentration at the time of the ingestion of the glucose, diminished this fall and also lessened or abolished the associated dumping symptoms.

Insulin was also shown to have a similar effect in diminishing the fall in plasma volume and abolishing dumping symptoms after a meal rich in carbohydrate. The hypothesis is put forward that the essential factor in the production of the dumping syndrome is a defect of carbohydrate metabolism, as a result of which the glucose tolerance curve is of the lag type and glucose absorption is relatively slow. This results in an increased osmotic transfer of fluid into the intestine, causing a large fall in plasma volume which, in those patients sensitive to such a fall, gives rise to the dumping syndrome.

Traumatic Dislocation of the Hip in Children. K. S. Morton. Brit. J. Surg. 47:233-237 (Nov.) 1959 [Bristol, England].

Morton feels that the paucity of references in the literature gives no indication of the true incidence of traumatic dislocation of the hip in children. Reviewing the English literature, he found descriptions of 129 cases, and he summarizes the information gained from these. The records of the Vancouver General Hospital from 1936 to 1958 were searched for cases of traumatic dislocation of the hip in children, aged 16 years or under, and reports on 7 such children were found, all of whom had been admitted since 1949. It is suspected that the distribution of cases reflects the inadequacy of earlier records rather than the true yearly incidence.

After analyzing both groups, totaling 136 cases of traumatic dislocation of the hip, the author arrives at certain broad conclusions. Children of any age, within the limits defined, are susceptible, though the injury becomes distinctly more common as the child begins to walk and becomes more venturesome. Boys predominate in a ratio of 2.5 to 1. The typical mechanism of the injury, usually thought to be that of a weight falling on the back of a child in some sort of squatting posture, appears to be rather uncommon, in that only 5 to 27 suffered this type of stress, and 3 of these were in the author's recent series of 7 cases.

Although there is little information about the interval before reduction, there seems to be a trend to immediate diagnosis followed by manipulative reduction within hours. Manipulative closed reduction under general anesthesia has become uniformly successful, there being no open reduction reported since 1922. Recommendations regarding the period of immobilization and restricted weight-bearing, based on this series, are impossible, since after-care received little attention in the reports. Excellent results were achieved in 4 of 5 of the author's cases with 2½ to 7 weeks of immobilization, and in the 5th the result was excellent with no enforced immobilization whatsoever.

Fractures complicating the dislocation are uncommon—a total of only 7 in the 136 cases. Slipped upper femoral epiphysis occurred in 3 cases. In 3 of the fracture cases subsequent avascular necrosis occurred, so that the associated injury would appear to predispose to the necrosis. Sciatic nerve lesions too were uncommon, only one case being reported. Recurrence did not occur in the author's 7 cases, and has not been reported since 1938. Although it might be suspected that avascular necrosis would occur more easily in children than in adults, its incidence in children was 10% (none in the author's series); this was the same as reported by one investigator for adults, and others had cited a higher incidence for adults. It is suggested that perhaps prompt and accurate reduction may account for the low incidence of avascular necrosis, but because of insufficient numbers this cannot be proved.

No conclusions with respect to traumatic arthritis are possible on the basis of this review. It seems likely, however, that, since fractures are uncommon in association with the dislocation and since avascular necrosis occurs in less than 10%, traumatic arthritis can also be said to be uncommon as a complication of traumatic dislocation of the hip in children.

Combination of Familial Polyposis of the Colon with Other Hereditary Diseases, Particularly Mesenchymal Tumors. J. Wieberdink. Nederl. tijdschr. geneesk. 103:2598-2601 (Dec. 19) 1959 (In Dutch) [Amsterdam].

The author and one of his colleagues had noted that in patients with familial polyposis of the colon other neoplastic lesions occurred, and they thought that this might not be accidental. The author found that Gardner in 1951 and Gardner and Richards in 1953 were the first who called attention to the association of hereditary polyposis of the colon and mesenchymal lesions. He mentions a number of other reports on this concurrence and shows that in the literature there has been a tendency to refer to the concurrence of polyposis of the colon with mesenchymal lesions as Gardner's syndrome.

The first of the 3 patients the author describes had undergone subtotal colectomy and ileorectostomy on account of polyposis of the colon at the age of 23 years. About 2 years after the operation a nodule was noted in the surgical scar, and at the end of 3 years this had become enlarged to the size of a coconut and was removed. The surgical specimen was identified as a desmoid tumor. In the second patient a total colectomy was performed for polyposis of the colon. Here again a nodule developed in the scar which after 30 months had reached the size of 2 fists. At the time of removal of this growth, the abdomen was explored, and an even larger growth was found retroperitoneally, which had spread to the mesentery. An exploratory excision revealed that the tumor was a neurofibroma. A maternal aunt of this patient likewise had had polyposis of the colon and had died at age 29 from an enormous growth in the mesentery. The third patient in whom polyposis of the colon had been diagnosed by roentgenologic and rectoscopic examination had had numerous subcutaneous nodules during childhood, some of which had been removed, but she refused removal of presently existing nodules. The mother of this patient had died of cancer. One brother, who had died during the war, during childhood had had a number of nodules removed. Another brother had undergone resection of the colon for malignant degeneration of polyposis, and since then the following lesions had been diagnosed: desmoid tumor, lipoma, atheroma, fibroma, and fibrosis. Besides these 3 patients, the author treated 7 others, with polyposis of the colon, who belonged to 4 different families with hereditary defects.

Discussing the familial concurrence of colonic polyposis and mesenchymal tumors, the author suggests that the mutation of a gene or of 2 coupled genes might be responsible for this combination of lesions. Searching for a pathogenesis, he raises the question of a possible relationship with the syndrome of Peutz, which is characterized by polyposis of the small intestine and pigmented (melanin) spots of the skin and mucous membranes.

Late Results in Skin Melanoma Treatment. A. P. Shanin. Probl. Onc. 4:601-607 (no. 5) 1958 [New York].

The author reviews the results of different methods of treating skin melanoma published since 1917. The data show that many questions concerning radiation, surgical treatment, and combined radiation and surgical therapy in the management of skin melanoma are still far from being answered. Two hundred fifty-four patients with skin melanoma were treated at the Institute of Oncology of the Academy of Medical Sciences in the U. S. S. R. from 1926 to 1952. Sixty-seven (31%) of the 213 patients who were followed up survived more than 5 years. The best results were found in the group who underwent surgical treatment alone, 44.4% of them surviving more than 5 years. The results of surgical treatment alone were considerably better than the combined radiation-operation method. This is understandable, since the patients undergoing the combined treatment were in an advanced stage of the disease and, therefore, were not eligible for surgical treatment alone. The location of the melanoma has a prognostic value. The rate of 5-year survival was 53.2% when the melanoma was on the face, 29.2% in the lower extremities, 23.2% in the torso, 23% in the upper extremities, and 18.2% on the neck.

It is the author's opinion that regional lymph nodes must be removed in all patients having histologically established melanoma or even malignant nevi. Malignant nevi, as well as flat and warty tumors up to 6 sq. cm. in size, can be cured by short-focus x-ray therapy. With more extensive tumors of the verrucous and papillomatous types, short-focus x-ray therapy must be followed by surgical excision of a facial tumor, or by electrosurgical excision of tumors in other parts of the body. In extensive tumors, as in ulcerous forms with deep infiltration, teleradium therapy should be used in doses of 7,000 to 8,000 r before radical removal of the tumor. The author believes that in stages 1 and 2 the lymph nodes should be excised, together with healthy tissue around the tumor, to a depth of 3 to 4 cm. 2 or 3 weeks after removal of the tumor; in stage 3 enlarged lymph nodes should be given preoperative telecurietherapy up to 7,000 or 8,000 r. Furthermore, he believes that radium or telecurietherapy should be applied to the wound after radical removal of the lymph nodes and surrounding tissue, and that recurrent tumors should be treated by x-ray or teleradium therapy followed by radical excision.

Two Episodes of Cardiac Arrest in One Week: Full Recovery After Cardiac Massage. W. B. Fleming, J. T. Hueston, J. L. Stubbe and J. D. Villiers. Brit. M. J. 1:157-160 (Jan. 16) 1960 [London].

This paper records the history of a severely burned child whose heart stopped during general anesthetization for skin-grafting operations on 2 separate occasions. The arrest occurred on each occasion during the induction of endotracheal anaesthesia. From a consideration of the possible precipitating factors, it is concluded that the most likely cause was vagal stimulation during intubation. This case is compared with a remarkably similar one of double cardiac arrest, which occurred during the treatment of burns, recently reported by Finer and Nylen from Sweden. Study of both cases suggests that the severely burned patient becomes increasingly prone to cardiac arrest from vagal stimulation. The metabolic disturbance apparently potentiates the response to harmful viscerocardiac reflexes, and so unnecessary vagal stimulation should be avoided in these cases. If intubation is essential, the authors suggest that the administration of atropine might limit the effect of these vagal reflexes.

NEUROLOGY & PSYCHIATRY

Some Sensory Syndromes in Children: Indifference to Pain and Sensory Neuropathy. T. E. Ogden, F. Robert and E. A. Carmichael. J. Neurol. Neurosurg. & Psychiat. 22:267-276 (Nov.) 1959 [London].

The authors report on a 14-year-old girl and on 2 boys, aged 10 and 11 years, with the "sensory syndrome," a nonspecific clinical picture by which several etiologically unrelated conditions may manifest themselves in children. Its outstanding features are insensitivity or indifference to pain with failure to avoid noxious stimuli and repeated self-injury. There may be a marked susceptibility to infection with perforating ulcers of the feet, osteomyelitis, and loss of terminal phalanges of fingers and toes. Disorganized joints are common. The girl had congenital indifference to pain, a condition in which, as far as could be determined, her sensory apparatus was intact, but she failed to react normally to painful stimuli, such as multiple heavy pinpricks, heavy pressure on tendons, and extremes of cold and heat. The younger boy had progressive sensory radicular neuropathy, a sensory neuron degeneration in the distal parts of the extremities, which involved the feet more than the hands and which was progressive. It was clinically indistinguishable from hereditary sensory radicular neuropathy and may have represented a sporadic case of this disease. The older boy had nonprogressive sensory neuropathy, a widespread sensory neuron degeneration involving cranial and thoracic nerves as well as those of the limbs. The deficit was more scattered and asymmetrical than in the younger boy with the progressive disease. The causation of these diseases is unknown.

Peripheral Neuritis Associated with Discoid Lupus Erythematosus. C. S. Dorsey. California Med. 92:40-41 (Jan.) 1960 [San Francisco].

The author reports a case of associated peripheral neuritis and lupus erythematosus, which he believes to be the first in the medical literature in which such a complication does not represent a terminal stage. A 45-year-old woman, complaining of a skin eruption of 10 years' duration, involving the face and the neck, received a diagnosis of discoid lupus erythematosus and was treated with chloroquine (Aralen) in the daily dose of 500 mg. Some months later, after the loss of her husband and the marriage of her only son, the patient showed signs of reactive depression. Difficulty in raising her arms and in rising from a chair, a feeling of heaviness in the legs, and weakness and swelling of the lower extremities occurred. Laboratory and neurological examinations were negative. The only abnormality noted was areflexia of the upper and lower extremities. Moderate peripheral changes of denervated activity, consistent with a diagnosis of peripheral neuritis, were recorded in the muscles of the feet, the legs, and the thighs. The administration of Aralen was discontinued because of the suspicion (later proved to be unsound) that it might have caused the neuritis. The patient received 10 mg. of prednisolone daily, and a week later she was able to walk. The prednisolone therapy was interrupted after 3 weeks because of gastric distress; the patient was discharged and went to live with her married son. She no longer showed evidences of reactive depression. A neurological examination reported complete recovery from the peripheral neuritis.

The unusual feature in this case was the effect of emotionally charged events on the course of the lupus–neuritis association. The symptoms and signs of neuritis appeared after the patient lost her husband and was separated from her only son. The fact that the patient's depression disappeared and that later her neuritis and lupus also abated is significant, although no definite cause-effect relationship can be demonstrated.

Catamnestic Data on Conditions of Hypotonia in Early Childhood: Critical Evaluation of Differential Diagnosis of Infantile Spinal Progressive Muscular Atrophy (Wernig-Hoffmann's Disease—Amyotonia Congenita Oppenheim). W. Horstmann. Ztschr. Kinderh. 82:649-667 (no. 6) 1959 (In German) [Berlin].

Generalized muscular hypotonia in infants involves diagnostic difficulties. The author points out that, soon after Oppenheim in 1900 published a preliminary report on atony of the musculature in early childhood (amyotonia congenita Oppenheim), some clinicians and pathologists raised objections, pointing out that Oppenheim's amyotonia congenita was probably identical with infantile spinal progressive muscular atrophy, which had been described by Werdnig in 1891 and by Hoffman in 1893 and which subsequently had been designated as Werdnig-Hoffmann's disease. Some investigators, however, agreed with Oppenheim that amyotonia congenita was a separate entity. Characteristics that have been cited as differentiating Werdnig-Hoffmann's infantile spinal progressive muscular atrophy from Oppenheim's amyotonia congenita are these: appearance of symptoms early in life; heredity; localized pareses, with circumscribed atrophies; absence of reflexes; signs of degeneration; progressive decline, sometimes interrupted by periods of arrest; and, finally, deficits in the bulbar functions.

The author investigated the reliability of these differentiating characteristics by a catamnestic analysis of the records of 38 children observed at the children's clinic of the University of Münster, in Westphalia, after 1925. The disorders of these children had been diagnosed as either Oppenheim's amyotonia congenita or as infantile spinal progressive muscular atrophy (Werdnig-Hoffmann), but the author groups all of them under this last item. In 10 of the 38 children the diagnosis of either amyotonia congenita or infantile spinal progressive muscular atrophy had been made by mistake. Three of these 10 had progressive muscular dystrophy; 2 had the atonic-astatic infantile paralysis of Foerster; 2 had hematomyelia; 1 had parainfectious hypotonia; 1 had hypotonia as a sequel of postvaccinal encephalitis; and 1 had an organic heart lesion and malformation of the brain. In the 28 children in whom the diagnosis was correct, the infantile spinal progressive muscular atrophy had become manifest in 7 shortly after birth, in 12 during the first 3 months, in 6 during the second 3-month period, and in 3 after the 6th month. Nineteen of the children died during the first year of life. There was usually a direct relationship between the time the disorder became manifest and the life expectancy of the patients, in that the course was usually the shorter, the earlier the defect had become manifest.

After commenting on the symptomatology, the author says that no evidence was found that Oppenheim's amyotonia congenita and Werdnig-Hoffmann's infantile spinal progressive muscular atrophy are distinct entities. Heredity can be proved in early as well as late cases; true remissions do not occur; life expectancy is short; and signs of degeneration and of involvement of the cerebral nerves can all be observed in both conditions. Furthermore, it has been demonstrated recently that the lesions do not differ morphologically. The author recommends that the term "infantile spinal progressive muscular atrophy" be maintained for both Werdnig-Hoffmann's and Oppenheim's diseases.

The Seasonal Incidence of Onset and Exacerbations in Multiple Sclerosis. K. Schapira. J. Neurol. Neurosurg. & Psychiat. 22:285-286 (Nov.) 1959 [London].

The author reports on 514 patients with multiple sclerosis, who were examined by him personally in the northeast of England; in 246 of these the onset of the disease could be clearly dated, and 268 had identifiable acute exacerbations. There was little difference in the incidence per month of initial attacks. More exacerbations, however, occurred in July than in any other month, but this increase in July was balanced by a decrease in June and August. When the incidence for 3-month periods throughout the year was compared, there was no evidence of seasonal preponderance either for total attacks (January to March, 130; April to June, 120; July to September, 131; October to December, 133) or for initial attacks or exacerbations.

GYNECOLOGY & OBSTETRICS

Chemotherapy for Carcinoma of the Uterus. J. C. Bateman, H. N. Carlton and J. P. Thibeault. Obst. & Gynec. 15:35-42 (Jan.) 1960 [New York].

This report is concerned with 46 patients in whom chemotherapy was employed for neoplasms of the uterus. Thirty-nine of the women sought help for advanced carcinoma that was recurrent after other forms of therapy; 2 had far-advanced inoperable carcinoma; and 5 were given chemotherapy postoperatively because of incompletely resected carcinoma. The chief chemotherapeutic agent employed was triethylene thiophosphoramide (ThioTEPA), a polyfunctioning alkylating agent similar in action to nitrogen mustard, but lacking the vesicant and nauseating characteristics of the latter. Crystals of this drug were dissolved in pyrogen-free water, 10 mg. per milliliter, and sterilized by passage through a Seitz filter. This solution, when stored in a refrigerator, was found *not to have lost its potency after 3 months.* Therapy consisted of maintenance treatment with ThioTEPA introduced into the tumor site at 1-to-2-week intervals by the transabdominal or transvaginal route in the majority of cases. Intravenous administration was employed in 3 patients with pulmonary metastases, and in 1 apprehensive patient. Intrapleural injection was given for pleural metastases in 1 patient, and oral medication was employed in 2 others for limited periods. In an effort to potentiate the chemotherapeutic action, supplementary therapy was tried with a nucleoside of puromycin in 7 cases and with actinomycin D in 3 cases. One additional patient received actinomycin D only.

The initial dose of ThioTEPA was determined by the patient's general status. Persons in whom renal excretion could be presumed to be slowed by age, debility, and/or cardiovascular renal disease were given one-half to two-thirds the dose generally employed (i. e., 60 mg. for local injection). Subsequent dosage in all cases was guided by the level of the white blood cell count done immediately prior to treatment. Dosage of the drug was reduced in response to a falling white blood cell count and usually omitted if the white blood cell count dropped to 3,000 or lower per cubic millimeter; treatment was resumed when the count rose. In patients receiving actinomycin D, it was found desirable to follow closely the platelet count as well as the white blood cell count. Supplementary therapy with small doses of cortisone (10-25 mg. once or twice daily) and long-acting adrenocorticotropic hormones injected at the time of chemotherapy was employed in the majority of cases. These agents tended to protect hematopoietic integrity as well as general well-being and appetite. Testosterone, even when given to the point of producing signs of masculinization, was less effective.

Antibiotics were used in the presence of symptomatic infection. Blood transfusions usually were administered when the hemoglobin value dropped below 7 Gm. per 100 cc.

Maintenance therapy with ThioTEPA appeared to prolong useful survival time in the majority of patients; in some instances this was impressive. Although objective regression of tumor was limited, tumor progression seemed to be slowed. In 2 cases partial regression of pulmonary metastases was demonstrated. The use of chemotherapy in early cancer of the uterus is indicated to improve survival time and reduce the incidence of late recurrences.

Müllerian Mixed Sarcoma (Sarcoma Botryoides of the Cervix. S. L. Marcus. Obst. & Gynec. 15:47-57 (Jan.) 1960 [New York].

The author suggests the term "müllerian mixed sarcoma" for the very rare and highly malignant lesion derived from müllerian duct mesenchyme. The tumor may contain a combination of fibrous or myxomatous elements, smooth muscle, striated muscle, cartilage, fat, or bone. The term "sarcoma botryoides" describes the grape-like appearance, but not all müllerian mixed sarcomas present this characteristic. Nevertheless, the term "botryoid" is sufficiently descriptive that it persists despite much criticism. The designation "carcinosarcoma," while connoting the combination of a malignant epithelial component with the sarcomatous element, does not suggest its histogenesis. The expression "mixed mesodermal tumor" is unsatisfactory, since it indicates neither its malignant nature nor its müllerian origin. Mixed mesodermal tumor could also be applied to Wilms's tumor of the kidney and to certain soft-tissue sarcomas. While no single designation is completely satisfactory, the term "müllerian mixed sarcoma" is suggested because it indicates the müllerian origin of the tumor, its mixed histological characteristics, and its malignant nature.

The author reports the histories of 2 patients with müllerian mixed sarcoma. The first was an 18-year-old woman who complained of a tumor protruding from the vagina for 3 weeks and a blood-tinged vaginal discharge for 1 week. Examination showed a fungating, edematous, polypoid tumor arising from the posterior lip of the cervix and nearly filling the vagina. The clinical impression of müllerian mixed sarcoma was confirmed by biopsy. The tumor was removed by electrocautery through the vagina, after which total hysterectomy was performed with excision of the upper quarter of the vagina. The patient was well until 2 years later, when a hard, fixed mass was palpated in the right side of the pelvis. Laparotomy disclosed a mass between the leaves of the right broad ligament, which was excised along with the tubes and the ovaries. It showed a protean appearance microscopically, the most prominent feature being large islands of cartilage. Other areas suggested leiomyosarcoma and endothelioma. The patient died 4 months later, or 29 months after the onset of symptoms.

The second patient was a 16-year-old girl. Biopsy of a gelatinous polypoid mass arising from the anterior cervical lip revealed müllerian mixed sarcoma. Shortly after the biopsy, a total abdominal hysterectomy and bilateral salpingo-oophorectomy were performed. No spread to the corpus, tubes, or ovaries was demonstrable. The patient is alive and well 7 years later, and gives no evidence of recurrence. Only 5 other cases with 5-year survival have been reported.

Theories of histogenesis are discussed, with emphasis on the capacity of müllerian-derived stroma to differentiate into various mesenchymal derivatives. Various forms of therapy, including irradiation, conservative surgical approaches with or without irradiation, and several chemotherapeutic agents, have generally been unsuccessful. The vast majority of patients succumb within 2 years to extensive pelvic and extrapelvic spread. Early lesions should be treated by radical hysterectomy, with pelvic and inguinal lymph node dissection and removal of the upper half of the vagina. For more advanced lesions, exenteration procedures must be considered.

Studies in Various Strains of Staphylococcus Aureus in Maternity Hospitals in Helsinki, With Special Reference to Their Phage Patterns and Sensitivity to Antibiotics. I. Rantasalo. Ann. chir. et gynaec. Fenniae 48:449-461 (no. 4) 1959 (In English) [Helsinki].

The author studied Staphylococcus aureus strains obtained from the milk of 495 mothers and from swabs taken from the pharynx and axilla of their children. The material was obtained on 8 wards of 4 different maternity hospitals in Helsinki. In addition, 252 pharyngeal and nasal samples taken from the personnel of a hospital as well as from 94 patients with Staph. aureus infections were studied.

The number of cases in which the milk of the mother was infected with Staph. aureus strains varied, from ward to ward, from 50 to 71% and was higher than in a previous investigation conducted by the author (50%). In the smallest ward, where there were only 1 to 3 parturients at a time, the number of milk samples infected with staphylococci was only 26%. Swabs from the pharynx and axilla of the infants yielded Staph. aureus strains in 23 to 53% of the cases, while only 39% of the infants investigated in the previous study were affected. Specimens from the personnel of a maternity hospital yielded Staph. aureus strains in 49% of the cases.

When the identified Staph. aureus strains were analyzed with the aid of phage typing and antibiograms, it was noticed that certain phage patterns with the same kind of sensitivity to antibiotics occurred in the same wards. In a maternity hospital where the personnel circulated from ward to ward, a similar phenomenon was observed in the entire hospital. A considerable proportion of the strains obtained from the staff of this hospital belonged also to the same type; however, the student nurses who had not yet been working in the wards did not carry the characteristic strains. Of the Staph. aureus strains found in infants, only 35 to 48% belonged to the same phage-typing group as those detected in their mother's milk. This demonstrates that the mother and the child could often have been infected independently.

Staphylococci which were characterized by a distinctive phage pattern among healthy persons stationed or employed in the hospital were not found in the same proportion in patients with mastitis or pemphigus, indicating a difference in the virulence of the strains. Strains belonging to the third phage group, and resistant to antibiotics, dominated among the types found in patients with inflammations. Staph. aureus strains corresponding to phage pattern 80 have caused some cases of sepsis among infants during the time of this study.

Incurable Cancer of the Breast. E. Tonkes. Nederl. tijdschr. geneesk. 103:2595-2598 (Dec. 19) 1959 (In Dutch) [Amsterdam].

The palliative value of various treatments is discussed on the basis of observations of 21 patients with incurable mammary cancer. Temporary relief was obtained by oophorectomy in a number of women who had not reached the menopause. Adrenalectomy sometimes resulted in a further remission in women of this group. Hormone therapy was much less effective than these surgical interventions in the limited number of cases analyzed by the author. He regards it as especially noteworthy that metastases were sometimes found in the ovaries or adrenals removed from women with advanced mammary cancer.

Primary Carcinoma of the Vulva with Special Reference to Leukoplakia. M. Stening and P. Elliott. J. Obst. & Gynaec. Brit. Emp. 66:897-904 (Dec.) 1959 [London].

This report is based on a series of 52 patients with primary vulval malignancy, who were observed and treated at the Royal Prince Alfred Hospital (King George V Annex) in Sydney from 1950 to 1957. The ages of the patients ranged from 40 to 92 years, but more than two-thirds were between 60 and 80. The authors comment on the predominating presenting symptoms, the anatomic sites, the types of growths, the preexisting vulval disorders, classification, node involvement, survival statistics, operability, and surgical mortality. They consider the following factors as important: 1. More than two-thirds of the patients who had primary carcinoma of the vulva were in the late postmenopausal age (between 60 and 80 years of age). 2. Pruritus vulvae was the most frequent presenting symptom (76%), the pruritus usually being of long standing. 3. The anatomic site of the malignant lesion was the epidermis of the sexual skin in 83% of the patients. 4. The ulcerative form of carcinoma was seen clinically in 85% of the patients. 5. Histologically, the lesion was nearly always a well-differentiated squamous carcinoma. 6. The preexisting diseases in the affected vulva were most frequently leukoplakia (62%) and lichen sclerosus et atrophicus (12%).

The triad of pruritus, leukoplakia, and the epidermal type of the ulcerative form of squamous vulval carcinoma in the elderly patient would appear to be a relatively frequent clinical entity. The authors feel that, if leukoplakia is regarded as an important link, then it is as rational to submit the aged person with vulval pruritus and leukoplakia to skin biopsy as it is to perform diagnostic curettage for postmenopausal bleeding. In this series of patients skin biopsies were usually multiple.

Since leukoplakia appears to be the preexisting disease in the majority of cases of vulval carcinoma, it seems important to clearly define this entity. Any hyperkeratotic lesion of squamous epithelium, which is kept moist and occluded, may give a whitish or opaque appearance. In the vulva, hyperkeratotic lesions giving this appearance may be due to lichen sclerosus et atrophicus, to lichenified skin which may be secondary to chronic irritation or mycotic lesions, or to conditions which have been described as leukoplakia but in which the most important histological feature is an atypical epithelium. The unquiet or atypical epithelium is regarded as leukoplakia proper. Epithelial atypism shows considerable variation, from the early increase in activity of the basal cells of the epithelium and thickening and increased cellularity of the squamous epithelium to conspicuous penetration of the rete pegs onto the altered connective tissue of the dermis. Atypical epithelium may evolve with varying speed into cancer, but it may also remain stationary at any stage, so that the course is unpredictable.

The sequence of pruritus, leukoplakia, and atypical epithelium demands simple vulvectomy. In the further discussion of the surgical treatment, the authors say that they followed the technique of extended radical vulvectomy with regional lymphadenectomy, as devised by Stanley Way. Certain modifications were introduced as the series progressed. Adequate excision of the primary growth demanded at times excision of the anus (3 cases), resection of the urethra (9 cases), and wide and deep excision of the vaginal walls when indicated. There were no local recurrences in this series. Special attention was paid to the postoperative fixation of the urethra to obviate skin bridging over the meatus and the occurrence of stress incontinence.

Carcinoma of the Uterine Cervix: Interstitial Radioactive Colloidal Gold Therapy of the Lateral Pelvic Nodes. W. S. Baker. California Med. 92:25-30 (Jan.) 1960 [San Francisco].

The author reports on the interstitial use of radioactive colloidal gold (Au^{198}) in combination with radium in the therapy of cancer of the cervix. The isotope is assayed and diluted to bring the volume to 70 cc. Half of this volume is injected transvaginally into the parametrium on the right, and the other half on the left. The points of injection are the obturator space, the hypogastric region, and the iliac fossa, bilaterally. After the injection of both sides of the parametrium, the actual radioactivity is measured at the lateral pelvic wall with the help of an instrument called the Probitron, a specially designed probe scintillation counter equipped with a sensitive tip.

Forty-eight patients with cancer of the cervix (40 with stage 1 and 8 with stage 2 tumor) were treated with Au^{198} to increase the intrauterine radium. At the time this article was written, 37 of the patients with stage 1 and 6 of those with stage 2 lesions were living for periods that varied from one month to 5 years after the treatment. The 5 patients who died are considered to have had lesions much more advanced than the stage revealed by the pelvic examination. It is doubtful that a radical operation would have saved them. The author believes that the method of interstitial introduction of Au^{198} is proving to be an effective weapon for the successful control of most stage 1 and stage 2 and some latent stage 3 cancers of the cervix.

PEDIATRICS

Unilateral Kidney Disease with Hypertension in Children. K. Harnaes and M. Seip. Acta paediat. 49:28-38 (Jan.) 1960 (In English) [Uppsala, Sweden].

Three children, a 10-year-old girl, an 11-year-old boy, and a 9-year-old boy, were admitted to the children's department of Rikshospitalet in Oslo, Norway, for the treatment of severe hypertension caused by unilateral kidney disease. The girl and the younger boy had chronic pyelonephritis with secondary atrophy of one kidney. The older boy had a narrow segment in the right renal artery and an aneurysm in the renal hilus, as revealed by an aortogram. Nephrectomy was performed on the right kidney in the girl and older boy, and on the left kidney in the younger boy. In the 2 boys the blood pressure was restored to normal after the nephrectomy, but in the girl additional treatment with 0.25 mg. of reserpine had to be given every evening for 2 years to obtain a normal blood pressure.

The duration of the hypertension before the surgical intervention is probably of considerable importance for the prognosis. The older boy had had severe hypertension for at least 4 years before the nephrectomy was performed; yet, cases have been reported in the literature of cure by nephrectomy in patients who had had hypertension for considerably longer periods than this patient. Marked retinal changes do not exclude good postoperative results. In all 3 patients the retinopathy cleared up after the nephrectomy, and in the girl particularly the retinopathy had been of severe degree. Infection or diminished function of the other kidney has been considered a contraindication to nephrectomy. In the younger boy there were also signs of infection in the contralateral kidney, but it was presumed that this infection could be secondary to that which was present in the atrophic kidney and that a favorable response to intensive antibiotic therapy could be hoped for. Marked reduction of renal function in the contralateral kidney, however, must be considered an absolute contraindication to nephrectomy.

The necessity of obtaining an aortogram in all children with hypertension, the causation of which is not clear, is stressed. With adequate treatment, the prognosis of unilateral kidney disease with hypertension is better in children than in adults, but it is not always good.

An Epidemic of Adenovirus Pneumonia. L. M. Koch and H. H. van Gelderen. Maandschr. kindergeneesk. 27:402-410 (Dec.) 1959 (In Dutch) [Leiden, Netherlands].

The authors report observations on 27 children in whom virus pneumonia was diagnosed at the Children's Clinic in Leiden during the winter of 1958-1959. These cases occurred during a period when upper respiratory infections showed an epidemic prevalence, but the pneumonia was limited largely to young children, all but 3 being less than 7 years old. The diagnosis of virus pneumonia was mostly a clinical one, being based chiefly on the absence of leukocytosis and the failure of response to treatment with antibiotics. Adequate serologic studies could be carried out in 14 of the 27 children, and in 11 of the 14 an adenovirus infection could be demonstrated by a high or a significant rise in the complement-fixation titer.

The duration of the pneumonia varied greatly, ranging from 8 to 64 days, the average being 20 days. Elevation of temperature persisted for an average of 9 days. Twelve children showed a remittent type of fever, which varied with the 24-hour period between 37.5 and 40 C (100 and 104 F). Roentgenologic examination revealed a lobar process in 7, a perihilar one in 6, and a disseminated one in 12 of the children. The pneumonia was often severe, and 3 of the children died.

Nearly all the children came from families in which siblings and/or parents had respiratory infections, and many of the patients had a history of chronic or recurrent respiratory infections. In several children the feces contained blood, or subclinical melena existed. Postmortem examination in one case revealed bleeding erosions in stomach and intestine. The authors emphasize that, although the adenovirus type of respiratory infection is usually mild, in young children it may be dangerous.

Results of Prolonged Administration of Large Doses of Corticotropin (ACTH) in the Treatment of Rheumatic Carditis During Childhood. E. Eckler, J. R. Bierich, I. Koch and G. Buhr. Ztschr. Kinderh. 82:697-728 (no. 6) 1959 (In German) [Berlin].

This paper is concerned with observations on 45 children treated for rheumatic carditis at the Children's Hospital in Bremen since November, 1953. The group included 8 very young children, 20 ranging in age from 6 to 10 years, and 17 between the ages of 11 and 17. Corticotropin (ACTH) was used exclusively, mainly because it was more readily available to the authors than was cortisone. It proved effective experimentally and clinically, and one intramuscular injection daily was readily tolerated by the children. Secondary effects were not more severe than with corticoids, and the authors were concerned with the evaluation of a uniformly treated group. All the children have been observed for at least 2 years, and some for as long as 5 years, since treatment. Since 1956 the clinical observations of the cardiac murmurs have been supplemented by phonocardiographic studies. This method of study is particularly important in view of the controversy about the possible disappearance of organic heart murmurs. The electrocardiographic examinations included leads from the extremities and from the chest wall. Laboratory examinations were concerned with the blood picture, erythrocyte sedimentation rate, venous blood culture, electrophoresis, and antistreptolysin titer. All degrees of severity of rheumatic carditis were represented among these 45 children.

After 1955 corticotropin was administered in the form of a repository preparation. The best results were obtained when treatment was continued with large doses for at least 6 weeks, or until the essential signs of activity of the rheumatic process had subsided. After that the dosage was gradually reduced, in accordance with the behavior of the erythrocyte sedimentation rate. The initial dose was usually 60 units of corticotropin per estimated square meter of body surface. One injection of this dose, in the form of the repository preparation, produced an optimal corticoid level in the patient's plasma for from 12 to 15 hours. The administration of this dose for several days raised the corticosteroid level to values that were 2 or 3 times higher. For this reason it was possible to reduce the hormone dose at the end of several weeks to half of the initial dose, without reducing the therapeutic effect. With this mode of treatment, there were no "rebound" effects and no reactivations of the rheumatic process, as had been the case with lower doses in some of the patients treated when corticotropin first came into use.

The results of treatment were most favorable in children who were treated early during their attacks of rheumatic carditis, in that their hearts were found to be normal at the time of discharge. A rather high percentage of those in whom treatment was begun later still had cardiac defects, and these defects were most severe in those in whom treatment had been started very late. Cardiac decompensation, however, persisted in none of the children. All forms of carditis responded equally. The secondary effects of corticotropin therapy were generally insignificant. After discontinuance of the hormone therapy, the hypophysial-adrenocortical system never showed deficient stress adaptation. Follow-up examinations, which in most children extended over more than 2 years, revealed only one recurrence of carditis, no progress in existing cardiac lesions, and, in several cases, improvement or complete reversion to normal of residual defects.

Radiographic Follow-Up in Hypertrophic Pyloric Stenosis (After Medical and Surgical Treatment). O. Steinicke and M. Roelsgaard. Acta paediat. 49:4-16 (Jan.) 1960 (In English) [Uppsala, Sweden].

The authors report on 209 boys and 44 girls, all of whom had been treated in early infancy for hypertrophic pyloric stenosis in 2 hospitals in Copenhagen. Of the 253 children, 80 had been treated surgically and 173 had been treated medically with spasmolytics. These patients were between the ages of 5 and 22 years when they underwent a roentgenographic follow-up examination in the roentgen-ray department of the Copenhagen County Hospital, Gentofte, Denmark, in an attempt to assess the conditions in their stomachs. The results of roentgenography of the stomach during the years of childhood revealed a decreasing incidence of sequelae of pyloric stenosis according to such criteria as abrupt transition from the proximal portion of the antrum to the distal 1 to 3 cm. of the prepyloric region, persistent narrowing of this region even at maximum filling, and reduced or arrested peristalsis in this region. For the medically treated, the tendency to normalization seemed to cease about the age of puberty, after which time about 13% of the patients had persistent roentgenographic changes. Since the surgical group comprised only children up to the age of 11 years, one cannot decide as yet whether similar conditions prevailed for the patients who were operated on. The results of the roentgenographic follow-up examination, however, showed that the tendency to normalization started at an earlier age in the surgically treated group than in the medically treated group.

A contratest group, comprised of 100 children with intestinal colic, was examined roentgenographically to obtain an estimate of the prepyloric region among children with no history of pyloric stenosis. In only one of these patients were roentgenographic changes observed in the stomach of the type designated as sequelae of hypertrophic pyloric stenosis. Of the 253 patients with previous hypertrophic pyloric stenosis, 18 (7%) had roentgenographic signs of peptic ulcer or gastroduodenitis, a ratio which hardly exceeded that to be expected in a normal population with a similar age distribution. These data suggest that the abnormalities in the prepyloric region, designated as sequelae of hypertrophic pyloric stenosis, are not caused by inflammatory changes in the stomach.

The results of this roentgenographic follow-up of children who had been treated for previous hypertrophic pyloric stenosis revealed a considerably lower incidence of sequelae of this condition in the acute phase than that found in a previously examined series of untreated patients. These findings stress the importance of early active treatment of hypertrophic pyloric stenosis. They also suggest that surgical treatment may be the method of choice.

Control of Lipemia in Children with Diabetes Mellitus: The Role of Insulin and the Effects of a Diet Rich in Unsaturated Fatty Acids. H. B. Salt, O. H. Wolff, A. Nestadt and J. K. Lloyd. Lancet 1:71-75 (Jan. 9) 1960 [London].

A study on the control of lipemia in 14 children, 2 to 14 years of age, with diabetes mellitus of varying duration is reported. In 4 previously untreated children, insulin therapy lowered the initially high values for serum triglyceride, beta-lipoprotein lipid, esterified fatty acid, and phospholipid to normal within 24 to 48 hours. In one of the patients in whom the serum cholesterol level was initially high, insulin brought it down to normal. In 4 patients under established diabetic control, observations of the diurnal variations of the various serum lipid and blood sugar levels revealed a relative constancy of the lipid levels in the face of considerable variation in blood sugar. In 13 diabetic patients under insulin control, the effects of feeding unsaturated fats on the serum lipid values were observed. Eight patients were given an emulsion of sunflower-seed oil; this led to a lowering of serum beta-lipoprotein lipid, esterified fatty acid, phospholipid, esterified cholesterol, and triglyceride concentrations to levels below the control levels. Five patients were given a diet in which most of the usual (animal) fat had been replaced by corn oil. The isocaloric change from the control to the corn-oil diet led to a fall in esterified cholesterol and beta-lipoprotein lipid values to about 60% of the initial control levels, in esterified fatty acid values to about 75%, and in unesterified cholesterol and phospholipid values to about 80%. In 2 patients on corn-oil diet the effects of lessening the insulin dosage were observed. The cholesterol and phospholipid values remained at low levels, but the diet did not prevent a rise in triglyceride, esterfied fatty acid, and omega (chylomicron) lipid fractions.

The authors point out that the hyperlipemia of diabetes has similarities to that preceding atheroma in older nondiabetic subjects. It may play an important part in the causation of the vascular complications. Hyperlipemia could be prevented by perfect control of the diabetic process with insulin; but such control, however desirable, is rarely if ever maintained for long periods. As an additional controlling measure, a diet rich in unsaturated fatty acids deserves a long-term trial.

DERMATOLOGY

X-Rays vs. Other Modalities in the Treatment of Acne Vulgaris: A Review of 1,265 Cases. S. C. Way. A. M. A. Arch. Dermat. 81:103-109 (Jan.) 1960 [Chicago].

The records of 1,265 patients who complained of acne vulgaris were reviewed by the author from the standpoint of etiology and of therapeutic results. The records of 265 patients were discarded, since the duration of treatment was insufficient for evaluation purposes; conclusions are drawn on the remaining 1,000 cases. The author believes that tension in its various forms, although often obscured, is an important, underrated cause of acne. Its effect upon the skin is more or less indirect, as it is capable of disturbing the body metabolism, including the endocrine balance. This importance of tension as a causative factor in acne is substantiated by the fact that patients, while on a pleasure trip, can often eat with impunity certain foods that have been known to cause exacerbations at home. Although 8% of the patients suffered from various forms of allergy, this figure represents a low normal. Special diets, in which offenders such as milk or its by-products, chocolate, oranges, nuts, grapes, and foods high in iodine content were eliminated, were helpful.

The therapeutic results obtained in patients treated after 1945, especially in the group not subjected to irradiation, speak well for the effectiveness of such new modalities as the sulfonamides, antibiotics, hormones, and steroid-containing lotions. Recent observations seem to indicate that the cystic type of acne should be studied from an allergic as well as an endocrine standpoint. Evidence is lacking to justify the use of x-rays in the management of acne vulgaris, unless other methods prove ineffective.

Griseofulvin, Clinical and Experimental Studies. H. M. Robinson Jr., R. C. V. Robinson, E. S. Bereston and others. A. M. A. Arch. Dermat. 81:66-80 (Jan.) 1960 [Chicago].

A study on the effect of griseofulvin, administered orally to 53 patients with tinea capitis, to 24 patients with onychomycosis, to 5 patients with tinea cruris varying in duration from 6 months to 15 years, to 14 patients with tinea corporis, and to 18 patients with tinea pedis due to Trichophyton rubrum, T. mentagrophytes, or Epidermophyton floccosum, is reported. The authors found that a total daily dose of 25 mg. of griseofulvin per kilogram of body weight is adequate in children up to 12 years of age; in adults, the optimum daily dose varies between 750 mg. and 1 Gm. The results obtained in the patients with tinea capitis indicate that eradication of infection may be obtained in 5 weeks in infections due to Microsporum audouini or M. canis. The criterion for cure must be a negative culture. In the treatment of onychomycosis, clinical improvement first becomes apparent in fingernail lesions in 3 weeks and in toenail lesions in 5 to 8 weeks. It is possible to obtain a positive culture of the offending organism from the distal ends of the nails even when growth is almost complete. All 24 patients with onychomycosis, in whom treatment with griseofulvin was initiated, were still under therapy at the time of this report. It was estimated that a minimum period of 5 months of continued treatment will be necessary to eradicate completely onychomycosis in fingernail lesions and a much longer period will be necessary to produce a satisfactory result in toenail lesions.

Relief of subjective symptoms was obtained in 48 to 72 hours, regardless of the causative organism or the duration of the condition, in the patients with tinea cruris. Objective improvement began in approximately one week, and involution of lesions was complete in from 4 to 6 weeks. It was possible to obtain positive cultures of the offending organism from each of the patients until all clinical signs had disappeared. In the treatment of tinea corporis, griseofulvin produced relief of subjective symptoms in from 1 to 5 days in all the patients, regardless of the causative organism or the duration of the condition. Involution of the lesions was complete, and cultures were negative in all the patients after 4 to 9 weeks. Relief from subjective symptoms was obtained within 5 to 14 days in the patients with tinea pedis. Clinical improvement was also noticed after 2 weeks of griseofulvin therapy. It was possible to obtain positive cultures of the offending organism from all the patients until all clinical signs had disappeared. Response to therapy in the treatment of tinea pedis is not as dramatic as in tinea corporis or tinea capitis. The toxicity studies performed during the course of this investigation indicate that this is a relatively nontoxic compound.

The authors conclude that griseofulvin is effective on oral administration in the treatment of superficial mycoses due to M. audouini, M. canis, T. rubrum, T. mentagrophytes, and E. floccosum. Clinical and experimental studies indicate that griseofulvin is fungistatic rather than fungicidal in action. The blood levels obtained by spectrophotometric examination, with butyl acetate as an extractant, are very low. Preliminary in vitro studies suggest that dermatophytes which are susceptible to the action of griseofulvin may eventually develop resistant strains.

Treatment of Tinea with Fulvicin (Griseofulvin). M. Nierman, D. M. Cohen and M. Golden. Illinois M. J. 117:1-5 (Jan.) 1960 [Chicago].

Griseofulvin (Fulvicin), in divided and gradually reduced doses of 1 or 2 Gm. daily, was given to 72 patients with tinea of the scalp, nails, or glabrous skin. Several patients had been afflicted for years, and none had responded satisfactorily to any previous attempts at therapy. Treatment was continued from a minimum of 2 weeks in tinea capitis or tinea corporis to a maximum of 14 weeks in onychomycosis. The patients were examined at frequent intervals during therapy and were followed for at least one month after discontinuance. Fungal infection responded rapidly to the treatment in all 72 patients. Therapy was continued until there was complete laboratory and clinical evidence of eradication. The patients with Microsporum audouini infections of the scalp responded within an average of 4 weeks, and tineas of the smooth skin were cured within 3 to 10 weeks. In onychomycosis, therapy for 3 or 4 months prevented invasion of the newly growing nail by fungi from the previously infected portions.

Two recurrences were observed among the 16 patients with tinea capitis due to M. audouini. In both instances low doses of Fulvicin had been used, because only minimal evidence of the disease had been observed before therapy. One patient, aged 8 years, appeared cured (cultures and Wood's light examinations negative) after 3 weeks of treatment with 500 mg. of Fulvicin daily. His brother, aged 6 years, had had more extensive involvement and was given 1 Gm. daily. The first child had a recurrence one month after cessation of therapy, and the sibling was reinfected. Permanent cure was achieved in both children with resumed dosage of 1 Gm. daily. The second recurrence was in a child, the youngest of 4 siblings with tinea capitis, who had presented a minimal case and received treatment for 2 weeks with 500 mg. daily. The other children had received higher amounts for longer periods of time. The youngest child had a relapse after one month, reinfecting another sibling; both were cured when therapy was resumed at 1 Gm. daily. Headache was the only untoward side-effect observed in this series; normal physiological values were unaffected.

Protection from Ultraviolet Carcinogenesis. J. M. Knox, A. C. Griffin and R. E. Hakin. J. Invest. Dermat. 34:51-58 (Jan.) 1960 [Baltimore].

The authors cite evidence obtained by other investigators to the effect that the incidence of cancer in different regions of the skin is roughly proportionate to the amount of sunlight reaching those regions, and that sunlight is a major cause of skin cancer. In the Southwest outdoor workers receive large amounts of solar radiation, and skin cancer of both the squamous and the basal-cell type is quite common in such persons. Topical sun screens have been applied to the skin to prevent sunburn in swimmers, sun bathers, fishermen, etc., but have not been generally recommended for protection from ultraviolet carcinogenesis. Various substances of the benzophenone family have been shown to be excellent sun-screening agents; therefore, a representative benzophenone, 3-benzoyl-4-hydroxy-6-methoxy-benzenesulfonic acid (BSA), was chosen for evaluation as to its ability to prevent the development of ultraviolet-induced skin cancers in albino mice. In selected experiments BSA was compared with *p*-aminobenzoic acid (PABA), the experiments demonstrating that ultraviolet carcinogenesis can be reduced by the topical application of BSA or PABA.

These findings in experimental animals may or may not be applicable to man. Physicians should probably begin by recommending a good sun screen for fair-skinned patients who are chronically exposed to sunlight. For once the process of ultraviolet carcinogenesis is initiated, it proceeds without further exposure, and damage that has already been done cannot be reversed. Moreover, in many persons it is important to prevent additional damage. The earlier the protective measures are instituted in susceptible persons, the less prone they should be to develop actinically induced skin cancer.

Ecthyma Contagiosum ("Orf"). U. W. Leavell Jr. J. Kentucky M. A. 58:42-44 (Jan.) 1960 [Louisville].

Ecthyma contagiosum, or orf, is a contagious viral disease in sheep which may be transmitted to man. In sheep the disorder begins as a vesicopustular eruption of the mouth and genital regions. The lesions form a dry crust and heal in 3 or 4 weeks. The virus, which has been found in crusts and seropurulent material, is resistant to drying and freezing and remains viable for long periods. The infection occurs shortly after the lambs are put on pasture in the spring. A few lambs will become infected from dried crusts on the pasture in which the virus from the previous season is still viable, and within weeks orf will become epidemic among the lambs.

The author describes the histories of 2 patients with orf. The first patient was a 31-year-old farmer with a tumor-like lesion on his temple, which had started as a small red spot that had spread after scratching. The lesion was excised, and the base cauterized. The area healed uneventfully, with little scarring, in about 2 weeks. The second patient, a 41-year-old woman, had a lesion on her finger. It was excised for microscopic examination, and the base cauterized. The area healed in 2 weeks. The 2 patients lived in different counties in Kentucky. Their farms were approximately 40 miles apart. In both cases there was history of exposure to lambs that had eruptions around their mouths. However, the wife and 3 children of the first patient did not experience any breaking out; the husband and 2 children of the second patient had no skin trouble. This suggests that the disease is not very contagious from one human to another.

The only significant pathological difference between human and animal infection in ecthyma contagiosum is the more acute inflammatory infiltrate in the latter. The epidermal changes are similar. In the case of the farmer, the question of differentiation between orf and milker's nodules arose. In orf there is a history of exposure to sheep that have infections of the skin of the mouth and nonhairy areas. In milker's nodules there is exposure to cows with warts on the udders.

Antifungal Activity of Griseofulvin. R. C. V. Robinson, H. M. Robinson Jr. and E. S. Bereston. South. M. J. 53:73-76 (Jan.) 1960 [Birmington, Ala.].

The authors report clinical, in vitro, and in vivo studies on the antifungal activity of orally administered griseofulvin. The sources of patient material included the University of Maryland Hospital outpatient department, Baltimore, and the authors' private practice. The mycoses treated were tinea capitis, tinea corporis, tinea cruris, onychomycosis, and tinea pedis. All diagnoses were confirmed by laboratory studies. The daily oral dose in 96 children with tinea capitis was 25 mg. per kilogram of body weight, or a total daily dose of from 250 to 750 mg. Normal growth of hair began in every child by the 3rd week and was complete at the end of 5 weeks. There were no therapeutic failures. Four children with tinea capitis due to Microsporum audouini returned with fresh lesions 1 to 3 months after therapy was stopped. Since the locations differed from those of the original lesions, these lesions were probably reinfections rather than relapses. All patients responded to second courses of griseofulvin. The feasibility of treating tinea capitis with a single massive dose of 3 to 5 Gm. of griseofulvin is being investigated. Nine patients have been treated in this manner with successful results in 8 of them.

The 55 patients with tinea cruris were treated with daily doses of 1 Gm. of griseofulvin, and involution of lesions required from 3 to 5 weeks; the 3 patients who had recurrences after treatment was stopped responded to a second course of griseofulvin. Griseofulvin was given to 46 patients with tinea pedis in daily doses of 1 Gm., involution occurring within 8 to 10 weeks; to 49 patients with tinea corporis in daily doses of 1 to 1.5 Gm., involution occurring within 5 to 6 weeks; and to 35 patients with onychomycosis in daily doses of 1 to 1.5 Gm., involution requiring an average period of 6 months.

Studies were undertaken to determine if dermatophytes would develop resistance to griseofulvin in vitro. Selected organisms were exposed to increasing concentrations of the drug in modified Sabouraud's dextrose agar. The fungi studied were Trichophyton mentagrophytes, T. rubrum, T. tonsurans, T. schoenleini, Epidermophyton floccosum, M. audouini, and M. canis, in strains which had not previously been in contact with griseofulvin. Evidence was obtained that these organisms apparently become resistant to griseofulvin, and it is deduced that resistance to the drug may also develop in vivo. There is no apparent relation of in vivo therapeutic response and in vitro sensitivity to griseofulvin. A total daily dose of 25 mg. per kilogram proved effective in the treatment of experimental animal infections as well as in human infections. Griseofulvin could not be detected in tissues in measurable amounts by a spectrophotometer, but preliminary observations indicate that the spectrophotofluorometer is a more sensitive instrument for this purpose.

Neuronevomatosis. J. M. Cid and F. P. Llobet. An. cir. 24:131-144 (July-Sept.) 1959 (In Spanish) [Rosario, Argentina].

The subject of this report was a 35-year-old man who was born with diffuse neuronevi of the nodular, tumoral, and gigantic types. The growths involved all the body, from the scalp to the soles of the feet, the palms of the hands, and the finger tips; only the scrotum was spared. When the patient was born, he was diagnosed as a monster. Euthanasia was advised but refused by the family physician. The patient developed weak and epileptic. At the age of 35 the nevi were marked, and the nodules and tumors were very large; a tumor on the supraclavicular fossa, for instance, was the size of an adult's head. The back from the neck to the gluteal region was pachydermatous, with a melanoma on the right shoulder. The patient complained of great difficulty in breathing. Roentgenologic examination of the chest showed large pulmonary metastases. The right lung did not breathe; only the upper half of the left lung was functioning. The patient died of asphyxia. Autopsy was not permitted.

The anatomicopathological study was made on the following material: (1) a hairy nevus taken from the right arm; (2) a piece of pachydermic skin; (3) nodules from the abdomen, the hands, and the finger tips; and (4) a melanoma. All the lesions, regardless of location, were neuronevi of a classical histological structure. The melanoma proved to have its origin in malignant transformation of the Schwannian symplasm and fusion of the symplasm with nests of superficial epithelioid cells which had migrated into the deep structure of the neuronevi. This abnormality, as well as phakomatosis, corresponds to the neuroectodermoses. Owing to the diffuse nodular and tumoral nature of the lesions and to the histological features in the case reported, the authors suggest the term "neuronevomatosis" for this rare abnormality.

UROLOGY

Selective Sacral Neurotomy for Hunner's Ulcer. T. H. Mason, G. L. Haines and B. W. Leversee. J. Neurosurg. 17:22-26 (Jan.) 1960 [Chicago].

The authors report on 4 women, between the ages of 49 and 68 years, with interstitial cystitis with ulceration (Hunner's ulcer), who were treated by selective sacral neurotomy at Ellis and St. Clare's hospitals in Schenectady, N. Y. The operation consisted of a midline sacral incision with reflection of the paraspinal muscles. After foraminal enlargement, the posterior branch of each of the second, third, and fourth sacral nerves was elevated on a blunt hook, and the anterior division was brought into view. After stimulation of each anterior nerve with a current of 60 cycles for 6 seconds, the response was measured with a catheter in the bladder and an attached cystometric recording device. The best response was noted with stimulation of the third sacral nerve, and the large anterior division of this nerve was ligated with silver clips and divided on each side. The wound was closed without drainage, and the indwelling catheter was left in place for postoperative cystometric recordings. Lasting relief from pain and frequency of urination associated with interstitial cystitis with ulceration was obtained in 3 of the 4 patients at the 18-month follow-up period; these patients felt that the results were gratifying. Stimulation at the surgical intervention seemed more practical than preoperative nerve blocking, which had been used by other workers. There were no detectable neurological residues from the root sections of the third sacral nerve, aside from change in bladder tone.

Problems of Lowered Alkaline Serum Phosphatase. G. Zinner and H. Ehrlich. Ztschr. Urol. 52:707-712 (Dec.) 1959 (In German) [Leipzig, Germany].

The authors determined the alkaline serum phosphatase level, according to the King-Armstrong method, in 500 patients in the urologic department of the Hospital Rudolfstiftung in Vienna. Of these patients, 129 had hypertrophy of the prostate; 21, carcinoma of the prostate; 3, neurogenic bladder; 5, stricture of the urethra; 90, ureteral calculi; 40, renal calculi; 20, lesions of the renal parenchyma; 8, cystopyelonephritis; 2, cystic kidneys; 8, hydronephrosis; 1, uremia; and 3, carcinoma of the bladder. The remaining patients had epididymitis, hydrocele, prostatitis, cystitis, and papilloma of the bladder. Normal alkaline serum phosphatase values range from 7.5 to 12 units. But values as low as 3 units were observed in patients with hypertrophy of the prostate and with stricture of the urethra (both conditions being associated with high values of residual urine) as well as in patients with occlusion of the ureter by calculi, in those with lesions of the renal parenchyma, and particularly in those with chronic pyelonephritis. The decrease in the alkaline serum phosphatase value may be caused by a damaging effect on the cells of the tubules and on the open border of the epithelial linings, both of which are carriers of the alkaline renal phosphatase. Contrary to these findings, an increase in the alkaline serum phosphatase value may be observed in patients with cardiac disease associated with liver damage. It may also be observed in patients with primary and secondary diseases of the bones, such as osteomalacia, osteitis fibrosa cystica, osteitis deformans, osteosarcoma, and bone metastasis.

Prophylactic Antimicrobial Therapy in Retropubic Prostatectomy. A. Marshall. Brit. J. Urol. 31:431-439 (Dec.) 1959 [Edinburgh].

This paper is concerned with the results of several investigations into the use of Sulphatriad (containing sulfadiazine, sulfamerazine, and sulfathiazole) and of various broad-spectrum antibiotics as prophylactics against infection in retropubic prostatectomy. A study of blood cultures in 50 patients after this operation had demonstrated an 82% incidence of bacteremia in the presence of infected urine and a 12.8% incidence with sterile urine.

Between December, 1956, and June, 1958, therapeutic studies were made on 100 patients, in groups of 10, picked at random. Alternate patients were given a 5-day course of penicillin (300,000 units twice daily) and Sulphatriad (first 2 Gm. and then 1 Gm. every 4 hours), commencing 1 or 2 days before operation. The other patients in this series received no prophylactic cover, but if any of them showed signs of infection, they received appropriate antibiotic therapy. Many of these patients had not been catheterized, and none had had more than a 6-day preliminary catheter drainage. In the author's department (Glasgow Royal Infirmary) a closed system of drainage is used, but some patients had received open drainage elsewhere. Alternate patients of a group of 17 who had received preliminary drainage for 7 days or longer, and who were considered to be grossly infected, were given either penicillin and Sulphatriad or only penicillin.

Forty patients with infected urine were studied as a consecutive series in order to assess the prophylactic value of various broad-spectrum antibiotics given after sensitivity tests. A 5-day course of the chosen agent was given, commencing 1 or 2 days before operation. The agents used were streptomycin, Chloromycetin, and Aureomycin. Blood culture studies were made before operation, immediately after enucleation of the prostate, and 1 and 2 hours after operation. Catheter specimens of urine were taken for culture immediately before operation.

It was found that bacteremia occurs frequently after retropubic prostatectomy in patients with infected urine despite "routine" prophylactic therapy with either Sulphatriad or streptomycin. Although no prophylactic cover seems necessary in sterile cases, in infected cases appropriate broad-spectrum antibiotics used as prophylactics against postoperative infection give better results than the routine use of either Sulphatriad or streptomycin. In infected cases appropriate broad-spectrum antimicrobials greatly reduce the incidence of postoperative bacteremia. It is of interest to note the association in some cases of a protracted bacteremia with very severe postoperative complications and prolonged convalescence. The fact that appropriate prophylactic therapy greatly reduces the incidence of both protracted bacteremia and severe postoperative infective illness suggests that bacteremia, when protracted, may be the initiating factor in such an illness.

Vasoligation for Prophylactic and Therapeutic Purposes. F. J. Pauer. Ztschr. Urol. 52:745-748 (Dec.) 1959 (In German) [Leipzig, Germany].

The author reports on 727 men who were permanently catheterized in the urologic department of the District Hospital in Graz, Austria. The catheter acts as a foreign body, favors infection, and may cause epididymitis. Of the 727 patients, 675 were, therefore, subjected to vasoligation, and 52 were not. Complications occurred in 13 (1.92%) of the 675 patients and in 38 (73.07%) of the 52 patients. In the 13 patients who had vasoligation, these complications consisted of stump infiltrates, and the patients obtained a complete cure. Of the 38 patients who did not have vasoligation, epididymitis occurred with abscess formation of the epididymis in 10; this necessitated removal of one testis in 9 patients and of both testes in 1.

In patients with acute epididymitis, rest in bed and elevation of the sex organs do not achieve complete immobilization of the inflamed organ; relief of pain and regression of the epididymitis may be obtained only slowly by conservative treatment, while in some patients abscess formation and loss of the testes may result. These observations have prompted the author to perform vasoligation even in patients with severe acute epididymitis and in those with inflammation of the vas deferens. By this surgical intervention, further afflux of bacteria will be inhibited; the peristalsis and antiperistalsis will be abolished to a considerable degree; and, thus, immobilization of the inflamed organ is supported. In all the patients undergoing vasoligation in this series, formation of an abscess was prevented, and the course of healing was considerably shortened. These are great advantages, which suggest that vasoligation should be employed on a large scale, particularly in severe cases with risk of formation of abscess.

OPHTHALMOLOGY

Congenital Vascular Veils in the Vitreous: Hereditary Retinoschisis. J. V. Balian and H. F. Falls. A. M. A. Arch. Ophth. 63:92-101 (Jan.) 1960 [Chicago].

The authors list the following as the essential characteristics of "congenital vascular veils in the vitreous": (1) translucent veil-like membranes projecting into the vitreous, carrying with them the retinal vasculature, which frequently exhibits ovate dehiscences and usually presents in the inferior temporal quadrant of the globe; (2) perivascular and intraretinal grayish opalescence, suggesting "reactive" or resolution gliosis; (3) macular aberration, which in the early stages of the disease presents retinal striae, suggesting central cystic retinoschisis, the latter being replaced by atrophic and pigmentary changes; (4) arborization of the peripheral retinal vasculature, which later may be lattice-like markings of the retinal substance; (5) fluidity and detachment of the posterior vitreous; (6) very rarely, "true" retinal detachment; (7) partial amblyopia in most affected persons, with or without strabismus; (8) high incidence of hypermetropia; (9) sex-linked recessive mode of inheritance; and (10) visual field defects in the form of central scotomas and/or peripheral suppression.

The disorder constitutes a rare but distinct clinical entity. Restricted to the male sex, this intraocular disease is apparently a sex-linked recessive trait. The authors describe the pertinent ocular findings of 6 afflicted members of 2 recently discovered families. Both families lived in southeastern Michigan and were of mixed Caucasian stock with no consanguinity. The authors also review the scant literature on congenital vascular veils in the vitreous. Three additional patients belonging to the second pedigree are mentioned, because they exhibited macular degeneration alone without vascularized veils. The authors believe, as Jager intimated, that the veils are nearly always accompanied by macular disease, while the converse is not true. They feel justified in including these 3 cases in the report, since it is most unlikely that 2 very rare retinal diseases would coexist in the family, and also because similar macular degeneration was observed by other investigators. The authors give support to the contention that this disease of the retina and/or macula is hereditary retinoschisis.

Collective Antibiotic Treatment of Trachoma: Report on Comparative Trials Leading to More Economic Methods of Treatment. J. Reinhards, A. Weber and F. Maxwell-Lyons. Bull. World Health Organ. 21:665-702 (no. 6) 1959 (In English) [Geneva].

With the assistance of the World Health Organization, a series of comparative trials, involving more than 9,000 children with active trachoma, have been conducted in the schools of Marrakech, Meknes, and Tiznit, Morocco, since 1953, in order to assess the value of local treatment of trachoma with chlortetracycline and to develop simple and economic methods of treatment for which there was a pressing need. Local application of a 1% chlortetracycline ointment 2 or 3 times daily for 60 days resulted in almost 80% cures under reasonably favorable conditions and in nearly 100% cures after retreatment of patients not cured by the first course. Equally good results were obtained by intermittent short-term treatment, i. e., local application of the chlortetracycline ointment twice daily for 3 consecutive days each month during 6 months. Relapse and reinfection rates were low. Collective mass treatment with antibiotics is clearly a valuable method of trachoma control. The use of intermittent treatment allows for a great economy both in antibiotics and in staff and other campaign expenses and makes possible the wide expansion of mass treatment programs.

Retinoschisis: I. Senile Type: A Clinical Report of 107 Cases. M. Shea, C. L. Schepens and S. R. von Pirquet. A. M. A. Arch. Ophth. 63:1-9 (Jan.) 1960 [Chicago].

Retinoschisis is a splitting of the retinal layers, which generally occurs in the outer plexiform layer. The authors present observations on 107 patients with senile retinoschisis, observed between 1946 and 1956. The group included 58 men with a peak incidence, between 50 and 60 years of age, and 49 women with a peak incidence, between 60 and 70 years of age. Since the retinoschisis was bilateral in most of the patients, the authors examined 178 eyes with senile retinoschisis with an indirect stereoscopic ophthalmoscope and scleral pressure. It was found that retinoschisis is not related to refractive error and is often asymptomatic. The lesions are usually of comparable extent in both eyes, and affect the temporal half predominantly with a predilection for the lower temporal quadrant. The ophthalmoscopic picture of the 3 stages of retinoschisis is described. The visual field loss is rarely noticed by the patient until splitting of the retina has gone as far as the equator. A permanent absolute field defect with sharp boundaries is observed; it progresses very slowly and may remain static for years.

The greatest danger is the development of retinal breaks in both layers of a retinoschisis with the subsequent appearance of a retinal detachment. Of 27 eyes which were followed for a minimum of 3 years, 6 eyes developed new breaks in one layer of the retinoschisis. In one eye, breaks subsequently appeared in both layers, and retinal detachment resulted. In 3 eyes, the retinoschisis extended further around the periphery; in 1 eye it extended posteriorly from the equator, but as yet has not involved the macula. The patient in whom retinal detachment developed was the only one subjectively aware of the progress of his condition. Retinal detachment developed also in 21 other eyes which initially showed breaks in both layers of the retina, and the detachment always originated in the area of the retinoschisis. The fact that retinal detachment developed in a total of 26 eyes with retinoschisis indicates that such eyes are predisposed to retinoschisis. Detachment is especially likely to occur in eyes in which the retinoschisis extends posteriorly to the equator.

Retinoschisis should be differentiated from retinal cyst, retinal detachment, and malignant choroidal melanoma. Prophylactic surgery in eyes with retinoschisis without retinal detachment was discontinued because of the poor results obtained by one of the authors.

The Pathologic Anatomy of Retinoschisis with a Report of Two Cases Diagnosed Clinically as Malignant Melanoma. L. E. Zimmerman and W. H. Spencer. A. M. A. Arch. Ophth. 63:10-19 (Jan.) 1960 [Chicago].

Cystoid degeneration of the peripheral retina (Blessig's cysts, Iwanoff's retinal edema) is observed so commonly that it has been regarded as a normal consequence of growth and aging. Throughout the peripheral retina, particularly on the temporal side, there occurs a more extensive type of retinal degeneration called retinoschisis. In this condition the typical Blessig-Iwanoff microcysts fuse and spread both circumferentially and posteriorly, splitting the retina in 2 leaves. The authors review the pathological anatomy of retinoschisis and report 2 unusual cases which demonstrate how this condition may confuse the examiner and lead to unnecessary enucleation.

In the first of these 2 cases there was no retinal detachment, the retinoschisis alone accounting for the tumor observed ophthalmoscopically. In the second case holes had developed in both walls of the split retina, and there was an associated detachment of the retina below the area of schisis. The authors believe that retinoschisis and the formation of discrete clear cysts in the peripheral retina are related to the much more commonly observed microcystoid degeneration of Blessig and Iwanoff. These share the following characteristics: an association with aging; frequent occurrence on the temporal side; circumferential progression along the peripheral retina; rare posterior extension; and mucoid degeneration, with accumulation of hyaluronidase-sensitive acid mucopolysaccharide in the lesions.

Neuro-Ophthalmologic Evaluation of Abducens Nerve Paralysis. E. C. Shrader and N. S. Schlezinger. A. M. A. Arch. Ophth. 63:84-91 (Jan.) 1960 [Chicago].

The survey presented by the authors has been designed to show the relative frequency of the various causes of isolated abducens nerve paralysis which the ophthalmologist is likely to see. The patient with an isolated abducens nerve paralysis is an entirely different diagnostic and prognostic problem from the one who exhibits abducens nerve paralysis in association with involvement of the other cranial nerves concerned with the ocular mechanism. For this reason, each patient in this series was completely evaluated from both ophthalmological and neurological standpoints. Patients with evidence of involvement of the olfactory, optic, oculomotor, trochlear, trigeminal, or facial nerves were excluded. Thus, the findings of papilledema, optic or retrobulbar neuritis, visual field defects, extraocular muscle paralysis exclusive of the lateral rectus muscle, objective evidence of ocular or facial sensory disturbances, or defects of facial musculature excluded a patient from the survey.

One hundred four patients with isolated acquired abducens nerve paralysis, which was first seen by the ophthalmologist, were studied primarily from the standpoint of etiology and prognosis. Almost 70% of the cases concerned patients over 50 years of age. The cases were equally divided in sex incidence and in lateralization of involvement, with 5 cases bilaterally affected. Diabetes mellitus was the etiological factor in 16 of the patients; multiple sclerosis, in 13; syphilis, in 10; neoplasm, in 7; neuritis, in 5; trauma, in 3; and miscellaneous causes, in 3 (1 case was probably due to Wernicke's encephalopathy, and the other 2 to ophthalmoplegic migraine). In 47 of the patients the etiology could not be definitely determined, but in 22 of these vascular factors seemed responsible, because all 22 had a systolic blood pressure over 180 mm. Hg and a diastolic pressure over 100 mm. Hg, all had evidence of generalized arteriosclerosis, and 8 had a cerebral vascular ictus and/or a myocardial infarction prior to the present episode.

If penicillin therapy were instituted before the 10th week of abducens nerve paralysis in a patient in whom the paralysis was due to syphilis, complete recovery was the rule. Specific therapy resulted in remission in a patient with sinusitis in 16 weeks, in one with allergic neuritis in 2 weeks, and in one with Wernicke's encephalopathy in 3 weeks. No case of isolated abducens nerve paralysis due to intracranial aneurysm could be proved in this series. In 10% of the cases no possible etiological factor was ascertainable.

THERAPEUTICS

Hidden Contacts with Penicillin. B. B. Siegel. Bull. World Health Organ. 21:703-713 (no. 6) 1959 (In English) [Geneva].

The extensive literature on immediate and delayed allergic reactions to penicillin suggests that this antibiotic has been the most common cause of drug allergy during the past decade. Patients who have experienced allergic reactions to penicillin have been warned to avoid further therapy with this drug. Despite attempts to follow this sound advice, these patients often continue to have reactions to penicillin as a result of unintentional and frequently unrecognized exposure to this antibiotic. The author discusses some of the main hidden sources of such contact with penicillin.

The most frequent of these hidden contacts with penicillin is the milk of cows. After a survey made in the United States in 1956, 5.9% of the samples of milk taken away from the market were found contaminated by penicillin in doses varying from 0.003 to 0.55 unit per cubic centimeter. Normal persons, who had been sensitized with the aid of serum containing penicillin reagents, have shown cutaneous reaction after the administration of a threshold dose of 40 units of crystalline penicillin G by mouth and after intravenous administration of a threshold dose of 12.5 units. Based on these observations in normal persons, it has been estimated that the amount of penicillin observed in samples of contaminated milk is more than sufficient to elicit clinical reactions in patients hypersensitive to this antibiotic. It may also be assumed that, if such doses are capable of producing clinical reactions in the predisposed person, they are also able, after continued and frequent repetition, to induce sensitization in this type of person.

The use of syringes which have been employed previously for the administration of penicillin is another cause of up to now unobserved antigenic contacts. The case of a 29-year-old patient is described in detail. This patient had received penicillin intramuscularly and by mouth in the course of 3 years preceding the administration of 25 mg. of an aqueous suspension of testosterone mixed with a small amount of 1% procaine hydrochloride for menstrual irregularity. A severe generalized reaction, with dyspnea, wheezing, vomiting, abdominal pain, and syncope, occurred within a few minutes after the testosterone injection. A thorough investigation showed that the reaction, first attributed to the drugs injected, was caused by a syringe contaminated with penicillin. Experimental studies show that it is practically impossible to destroy completely the antigenic principle of the antibiotic by boiling the syringes and that it is difficult to eliminate all traces of penicillin by the current procedures of sterilization. It would be advisable to reserve special syringes and a separate sterilizer for penicillin injections. A more desirable solution would be the employment of disposable cartridges *in penicillin administration.*

The unintentional inhalation of penicillin-contaminated air may induce acute symptoms in unusually sensitive patients. Of 11 patients with an immediate allergic reaction to penicillin studied by the author, 6 handled the drug fairly regularly. Hence, handling of penicillin may be an occupational hazard, not only by inducing epidermal hypersensitivity by contact but also by inducing constitutional hypersensitivity by inhalation, manifested by tightness and wheezing in the chest and shock. The interrogation of a patient for a history of allergy to penicillin should include questions on his previous exposure to penicillin in his present and past occupations. Furthermore, it would be advisable to warn patients known to be hypersensitive to penicillin to avoid those occupations in which inhalation of this antibiotic is likely to occur. Clinical and experimental observations are presented to show that the minimal amounts of penicillin contained in commercial poliomyelitis vaccine are sufficient to cause allergic reactions in sensitive persons.

Vascular Headache: Its Treatment with Sublingual Ergotamine Tartrate. L. S. Blumenthal and M. Fuchs. South. M. J. 53:47-51 (Jan.) 1960 [Birmingham, Ala.].

This report is concerned with observations on patients with recurrent headaches, who were selected from a larger, previously investigated series. A new saliva-soluble form of ergotamine tartrate was to be investigated in the therapy of vascular headache. Studies were made on 31 patients, 20 of whom were considered to have migraine headaches: 9, tension-vascular headaches; and 2, atypical facial pain of the histamine cephalalgia type. The majority were in the 20-to-40-year age group. Eighteen of the patients were women, and 13 were men. Each patient was instructed concerning the procedure to follow at the first sign of headache. These patients were well known to the investigators and had been previously treated with a variety of other medicaments.

For the treatment of an acute attack, the patient was advised to place a tablet containing ergotamine tartrate under the tongue and to refrain from eating, drinking, talking, smoking, chewing, or swallowing until the tablet had entirely disintegrated. At first, some experimental tablets which dissolved rather slowly were used to determine the relative importance of speed in sublingual disintegration. Tablets would remain in the mouth for as long as 15 and 20 minutes before dissolving. When it was found that rapid disintegration was essential, a new preparation was used, which required only 30 to 60 seconds to disintegrate and disperse on the sublingual surface. At the first sign of a headache the patient was to take 1 tablet (containing 2 mg. of ergotamine tartrate) and to repeat this dose every 15 minutes until the headache was relieved, or until a maximum of 3 tablets had been used.

Twenty-one of the 31 patients obtained complete relief, most of them from 2 to 4 mg. of ergotamine; 4 more obtained partial relief, and 3 temporary relief. Only 3 patients failed to be relieved by the administration of ergotamine, and 2 of these did not take the full recommended dosage. Twenty-six patients reported no side-effects, and 5 reported only mild nausea. This study demonstrates that the early sublingual administration of a highly soluble ergotamine tartrate tablet will often abort an impending attack of vascular headache or considerably reduce its intensity.

A Pharmacodynamic Approach to the Evaluation of Nitrites in the Treatment of Angina Pectoris. I. Hirshleifer. Am. J. Cardiol. 5:66-71 (Jan.) 1960 [New York].

The author subjected 60 persons, both normal and those with coronary sclerosis and insufficiency, seen in private practice and at Kings County Hospital Center in Brooklyn, N. Y., to examination with Winsor's highly sensitive segmental plethysmograph and, in some instances, to comparative electrocardiographic study. The effects of 2 vasodilators, glyceryl trinitrate and erythrol tetranitrate, were recorded after a single sublingual dose and a single oral dose. In all the persons tested, the pneumatic plethysmographic cuff was applied to the ankle. The plethysmographic records have offered direct evidence that, with glyceryl trinitrate and erythrol tetranitrate, sublingual and oral routes are essentially equivalent in producing the desired therapeutic effect. Sublingually administered glyceryl trinitrate tablets may take from 30 seconds to as long as 8 minutes to disintegrate. The more extended disintegration time is particularly true for older age groups. Although it is now generally believed that the sublingual form is preferable for these vasodilator agents, objective appraisal indicates that onset, peak, and tapering-off of induced dilatation are ostensibly the same after sublingual or gastric absorption of the drugs. From a subjective viewpoint, however, oral therapy is more desirable, since a tablet held under the tongue is rather unpleasant and imparts a continuous sensation of a serious need for medication.

These observations suggest that Winsor's segmental plethysmograph, by indicating volume changes with each cardiac pulsation, offers an opportunity for a truly objective pharmacodynamic approach to the evaluation of vasodilating properties of nitrites in patients with angina pectoris. Further investigations with this instrument, ideally suited to detecting effects on peripheral vascular beds, are currently under way.

Maintenance Treatment of Pernicious Anemia by Massive Parenteral Doses of Vitamin B_{12} at Intervals of 12 Weeks. J. D. Kinloch. Brit. M. J. 1:99-100 (Jan. 9) 1960 [London].

One hundred patients, who had been fully treated for pernicious anemia and were under regular medical supervision, were kept on a 2-year maintenance therapy, consisting of 1,000 mcg. of vitamin B_{12} given parenterally every 12 weeks. The hemoglobin level and the red blood cell count were estimated at least every 12 weeks; serum vitamin B_{12} assays were performed in most patients with samples obtained at random intervals of 1, 2, or 3 months after the administration. The results of this treatment were evaluated by comparing the mean of the first 3 and the mean of the last 3 red blood cell counts and hemoglobin estimations. The levels considered desirable to maintain were 100% hemoglobin and 5 million erythrocytes per cubic millimeter for men, and 90% hemoglobin and 4.5 million erythrocytes per cubic millimeter for women.

Eighty-seven patients were maintained on this trial therapy throughout the 2-year period and showed no deterioration in their red blood cell counts or hemoglobin values. Seventeen of the 87 were maintained with red blood cell counts slightly under the desired level, and 2 required an intermittent administration of iron to keep up the hemoglobin values. Thirteen patients were withdrawn from the experimental group because of unsatisfactory red blood cell counts, although in no case did the count go below 4 million per cubic millimeter. In these patients the administration of 1,000 mcg. of vitamin B_{12} was increased to an injection once a month instead of every 12 weeks. Serum vitamin B_{12} assays performed on the 87 patients whose maintenance condition was satisfactory showed that 18 months after the therapy was started the desired levels had been maintained except in one patient. It is concluded that, although the administration of 1,000 mcg. of vitamin B_{12} at 12-week intervals provides an adequate maintenance therapy for most patients with pernicious anemia, this dosage is inadequate for a small number of patients and cannot be recommended as a general routine procedure.

Diethylcarbamazine Therapy in Tropical Eosinophilia. K. Nath and S. N. Pandeya. Brit. M. J. 1:104-107 (Jan. 9) 1960 [London].

Forty-four patients with tropical eosinophilia were treated at the Ghandi Memorial and Associated Hospitals in Lucknow, India. Most of them had a typical history of dry cough, breathlessness, and pulmonary wheeze; the physical signs varied and consisted of harsh breathing with crepitations and rhonchi and different degrees of bronchial spasm. Six patients had no pulmonary symptoms. Roentgenographic and routine fluoroscopic examinations showed increased striation or mottling in the pulmonary field in most patients. In all of them the eosinophil count was more than 4,000 per cubic millimeter. Diethylcarbamazine was given in the form of tablets and in daily doses of 8 mg. per kilogram of body weight. A patient was considered cured when all the symptoms and signs had disappeared completely and the absolute eosinophil count had been lowered to 1,000 or less per cubic millimeter.

Forty patients (91%) were cured with diethylcarbamazine. Hematological response was only partial in the remaining 4 patients; in one of these there was no marked symptomatic relief. Complete or partial relief was observed as early as the 4th day of treatment. Concomitantly with the symptomatic improvement there was general clearing of the physical signs. The eosinophil count showed a definite fall which started within 4 days in 24 patients (54.5%). The duration of the therapy was 2 weeks in 81.8% of the patients; it was only 4 days in 1 patient, between 4 and 6 days in 3, and over 2 weeks in 8, including the 4 patients who were resistant to diethylcarbamazine therapy but who responded to oxophenarsine hydrochloride injections.

The treatment with diethylcarbamazine was fairly well tolerated. A few patients complained of nausea and loss of appetite, and 2 suffered from vomiting. Diethylcarbamazine was equally effective in relieving extrapulmonary manifestations of tropical eosinophilia, such as dry pleurisy, pleurisy with effusion, lymphadenopathy, abdominal pain, splenomegaly, and hepatomegaly. This treatment seems to be superior to the arsenic treatment, because it is easily administered, has a high cure rate in a relatively short period of time, and causes no dangerous reactions.

Treatment of Staphylococcal Septicemia with Vancomycin: Report of Thirty-Three Cases. W. M. M. Kirby, D. M. Perry and A. W. Bauer. New England J. Med. 262:49-55 (Jan. 14) 1960 [Boston].

Vancomycin was given to 33 patients with staphylococcic septicemia, who were observed over a period of 19 months (1957-1959) at King County Hospital and at 4 other hospitals in the area of Seattle. In all but one patient one or more blood cultures were positive for staphylococci before treatment was started. In the one patient whose blood cultures were not positive, multiple subcutaneous abscesses were present. Vancomycin was supplied as a powder in 0.5-Gm. ampuls, and 10 ml. of sterile distilled water was added to each ampul. This concentrated solution was further diluted in 100 to 200 ml. of 5% dextrose in distilled water and was administered as an intravenous infusion over a period of 20 to 30 minutes. Most patients received 1 Gm. every 12 hours for at least a week, and in many the dosage was decreased to 1 Gm. daily thereafter. In no case was more than 2 Gm. given in a 24-hour period. Twenty-two of the patients were over 50 years of age.

In 19 of the 33 cases, staphylococcic infections were acquired in the hospital by patients who had serious underlying diseases on admission. The sources of infection in these 19 cases consisted of aspiration pneumonia (4), wound infections (4), cut-down infections (10), and indwelling catheter (1). Most of the hospital-acquired infections occurred in elderly, debilitated patients, and were associated with major surgical procedures or with diseases requiring intravenous infusions through polyethylene catheters (cut-down infections). Staphylococci isolated from 27 of the 33 patients were resistant to 2 or more antibiotics. Twenty patients were cured, and a number of them responded well to vancomycin after they had failed to improve with other antibiotics to which the organisms were susceptible. Six patients were improved by vancomycin therapy but died of underlying disease, and 7 were classified as treatment failures, although most of these patients had overwhelming infections and died shortly after treatment was started.

When it was possible to test staphylococci isolated from patients after vancomycin therapy, they remained susceptible to the antibiotic. The chief limitation in the use of vancomycin is the necessity of administering it intravenously. Side-effects, consisting of chills, fever, and rashes, occurred in a small percentage of patients and could usually be controlled by slower administration and by the addition of antihistamines or steroids.

Neuropsychiatric Complications Following Chlorothiazide Therapy in Patients with Hepatic Cirrhosis: Possible Relation to Hypokalæmia. A. E. Read, J. Laidlaw, R. M. Haslam and S. Sherlock. Clin. Sc. 18:409-423 (no. 3) 1959 [London].

The orally active diuretic, chlorothiazide, when given to patients with liver disease who have experienced hepatic precoma, is likely to cause neuropsychiatric complications. It seemed of importance to ascertain whether hypopotassemia (hypokalemia) or some other factor was responsible for the neuropsychiatric deterioration. The authors accordingly made studies on 20 patients with Laennec's cirrhosis, 15 of whom were given chlorothiazide in a dose of 0.5 Gm. 4 times a day for an average of 17 days. Five patients were given potassium supplements throughout the period of treatment.

Chlorothiazide therapy was followed by the neuropsychiatric changes of impending hepatic coma in 7 of 15 patients with Laennec's cirrhosis of the liver. Six of these had a good diuretic response to the drug. The diuresis was accompanied by urinary potassium increase; serum potassium values fell; and the alkali reserve and blood pH rose. Patients showing neuropsychiatric changes had a rise in arterial blood ammonium values. The onset of hepatic precoma was marked by a gross slowing of the frequency of rhythmic activity in the electroencephalogram (EEG). Slight slowing was also noted in those who did not show clinical evidence of neuropsychiatric deterioration and in 2 subjects without liver disease.

Potassium supplements resulted in a return of the EEG toward normal and in clinical improvement even though chlorothiazide was continued. In 2 patients potassium supplements given with chlorothiazide prevented the development of neuropsychiatric changes. In a third patient the supplements were insufficient to prevent the serum potassium level from falling, and hepatic precoma developed. Potassium depletion induced by diet and exchange resins was followed by neuropsychiatric deterioration in 3 patients with cirrhosis. Hepatic coma developing after chlorothiazide therapy is related to potassium deficiency and its accompanying extracellular alkalosis.

In Vitro Activity of 1600 F.I. on 123 Strains of Staphylococcus Pyogenes Resistant to Various Antibiotics. P. Cocchi. Riv. clin. pediat. 64:257-263 (Oct.) 1959 (In Italian) [Florence, Italy].

A new Italian antibiotic preparation, isolated from a strain of Streptomyces organisms and marketed under the name of 1600 F.I., was tested by the author on 123 strains of Staphylococcus pyogenes. These strains, which had been obtained from human pathological tissue or nasal mucosa of healthy persons, were resistant to different types of antibiotics. Seventy-six strains were resistant to one of the following antibiotics: penicillin, erythromycin, tetracycline, oleandomycin, novobiocin, or 1600 F.I.; 33 strains were simultaneously resistant to various combinations of 2 antibiotics, 9 strains to 3 antibiotics, 4 strains to 4 antibiotics, and 1 strain to 5 antibiotics. None of the strains were simultaneously resistant to all 6 antibiotics. Resistance to penicillin was observed in 70% of the instances, to erythromycin in 14%, to tetracycline in 30%, to oleandomycin in 8%, to novobiocin in 17%, and to 1600 F.I. in 4%. The most active concentration of 1600 F.I. in vitro on various strains of staphylococci varied from 2 to 8 mcg. per cubic centimeter. The new antibiotic 1600 F.I. has thus proved to be an effective drug against many staphylococcic infections, including some that are resistant to other antibiotics.

Ventricular Fibrillation During and After Coronary Artery Occlusion: Incidence and Protection Afforded by Various Drugs. S. E. Stephenson Jr., R. K. Cole, T. F. Parrish and others. Am. J. Cardiol. 5:77-87 (Jan.) 1960 [New York].

The authors studied the incidence of ventricular fibrillation during and after temporary experimental occlusion of the left anterior descending coronary artery, or its branches, in 351 dogs. A standardized procedure of 30-minute temporary occlusion of this artery was employed in 330 of these dogs. There was usually a critical period, after 12 and up to 15 minutes, of ischemia, which was characterized by a tendency to arrhythmia, such as extrasystoles, singly or in runs, ventricular tachycardia, or both extrasystoles and tachycardia, if not a fatal ventricular fibrillation. Several instances of transient ventricular fibrillation were observed. Of 239 animals surviving 30 minutes of occlusion, ventricular fibrillation occurred in 169 (71%) immediately after release of the artery, while fibrillation developed in only 91 (28%) of the 330 animals during the occlusion. The reestablishment of blood flow to an area of the myocardium made ischemic for 30 minutes by occlusion of the anterior descending coronary artery is more likely to precipitate ventricular fibrillation than is the period of ischemia itself.

A variety of drugs were tested in 324 dogs to determine their protective action against the development of ventricular fibrillation during occlusion and after release of the ligature. Quinidine was the most effective drug in affording protection from ventricular arrythmia, which occurred in only 3 (7%) of 41 dogs during occlusion and in 18 (47%) of 38 dogs after occlusion. Procaine, procaine amide, and hydralazine (Apresoline) offered good protection during the ischemic period.

A reduced incidence of ventricular fibrillation on reopening the ligature also resulted from the administration of hydralazine in 11 (44%) of 25 dogs, and from the administration of phentolamine (Regitine) in 7 (37%) of 19 dogs. Of the other drugs tested, only one, Pendiomid, showed significant protection (an incidence of 52%). Paveril, adenosinetriphosphate, tolazoline (Priscoline), Trasentine, and lidocaine (Xylocaine) were of little value under the conditions of this study. Systemic arterial pres- arrhythmia. Electrical countershock accomplished cardiac resuscitation in 75% of the fibrillating dogs. From these experiments, quinidine appears to be the drug of choice in the prophylaxis of fatal ven- sures did not predict the onset of ventricular tricular arrhythmias.

PATHOLOGY

Intracranial Involvement from Carcinoma of the Lung. B. Halpert, E. E. Erickson and W. S. Fields. A. M. A. Arch. Path. 69:93-103 (Jan.) 1960 [Chicago].

The authors examined the clinical histories and autopsy records of 3,000 male patients who died in the Veterans Administration Hospital in Houston, Texas, between 1949 and 1958. Carcinoma of the lung was observed in 363 of these patients. After the brain had been examined in 338 of the 363 patients, intracranial metastatic involvement was recorded in 129 instances, comprising 38.1% of the brains examined. Of the 338 patients, 75 were 50 years of age or younger, and 263 were over 50. Involvement of the brain occurred in 41 (54.6%) of the 75 patients, and in 88 (33.4%) of the 263 patients. Accordingly, carcinoma of the lung involved the brain more frequently before the age of 50, and significantly less often after the age of 50. The cell type appeared to bear no significant relationship to intracranial metastasis, except that columnar-cell carcinomas metastasizing to the brain were relatively high and that more than 50% of the carcinomas involving the hypophysis were the reserve-cell type.

Among the 129 patients with intracranial metastasis, 30 (about 25%) had clinical signs and symptoms of intracranial involvement as the presenting complaint. In 51 additional patients, clinical manifestations of involvement of the central nervous system were recognized in the course of their illness. The condition of most of the remaining 48 patients went "rapidly downhill," and they died with no localizing symptoms recorded.

Serum Cholesterol Levels in Human Atherosclerosis. J. C. Paterson, L. Dyer and E. C. Armstrong. Canad. M. A. J. 82:6-11 (Jan. 2) 1960 [Toronto].

Serum cholesterol determinations have been carried out at least once a year on 800 ambulatory patients who were permanently confined to hospital with atherosclerosis. These determinations were begun in 1953, and by April, 1959, there were 191 fatalities in the series. Autopsy was performed on these patients, and the severity of the atherosclerosis was estimated in the abdominal aorta and in the coronary, cerebral, and femoral arteries by means of 6 different criteria: crude morphologic grading; measurement of the thickness of the largest plaque; and determinations of the total lipid content, lipid concentration, total calcium content, and calcium concentration. The mean ante-mortem serum cholesterol level for each patient was then compared with the severity of the disease in his arteries and with the presence or absence of those complications of atherosclerosis that can be detected at autopsy.

An adequate number of cases for statistical analysis were available only for those patients in the 7th, 8th, and 9th decades. The results lent little support to the contention that the severity of atherosclerosis is related to the level of serum cholesterol, except perhaps when this level exceeds 300 mg. per 100 cc. In 58 patients in the age group from 60 to 69 years, significant relationships between the level of serum cholesterol and the severity of atherosclerosis were found only once in 40 statistical analyses. The complications of atherosclerosis were just as frequent in patients with low serum cholesterol levels (150-199 mg. per 100 cc.) as in those with moderately high levels (250-299 mg. per 100 cc.).

Neurofibromatosis (Recklinghausen's Disease) and Pheochromocytoma. G. G. Schlegel. Schweiz. med. Wchnschr. 90:31-39 (Jan. 9) 1960 (In German) [Basel, Switzerland].

Of 25,274 autopsies performed at the pathological institute of the University in Zurich, Switzerland, between 1945 and 1958, a pathological diagnosis of neurofibromatosis (Recklinghausen's disease) was established in 13 cases (0.5 per 1,000), of pheochromocytoma in 23 cases (0.9 per 1,000), and of combined neurofibromatosis and pheochromocytoma in 2 cases (0.08 per 1,000). The evaluation of the data reveals a statistically significant increased incidence of neurofibromatosis combined with pheochromocytoma. The first of the 2 cases of combined neurofibromatosis and pheochromocytoma occurred in a 47-year-old woman who was a foundling and who from childhood had shown the typical aspect of the cutaneous form of neurofibromatosis. During the last years of her life she had complained of headache and repeated attacks of pain in the right epigastric region. Found unconscious, she was admitted to hospital as an emergency, with a blood pressure of 240/150 mm. Hg. Death occurred 4 hours later. Autopsy revealed an encephalorrhagia into the left corpus striatum, with perforation of the ventricle, and a pheochromocytoma, the size of a fist, of the left adrenal. The pheochromocytoma was the cause of the blood pressure crisis and of the fatal encephalorrhagia.

The second case was that of a 54-year-old man who from childhood showed the typical cutaneous neurofibromatosis, a distal defect of the shaft of the left tibia and fibula with formation of pseudarthrosis, and a high degree of bilateral weakness of vision. He also complained of headache for the past 10 years, and in the last year had had attacks of abdominal cramps and unconsciousness. He was found unconscious with a right-sided hemiplegia and, on admission to hospital, had a blood pressure of 220/110 mm. Hg; he died shortly after the admission. Autopsy revealed an encephalorrhagia into the left basal ganglions, with perforation into the left lateral ventricle, generalized neurofibromatosis with formation of nodules and cutaneous pigment spots, a glioma in the optic chiasm, and a neurofibroma in the shaft of the left tibia; as typical, additional findings, there were a pseudarthrosis of the left leg and an apple-sized pheochromocytoma of the left adrenal.

Pheochromocytoma is a rather rare, but nevertheless highly typical, accessory finding in patients with neurofibromatosis. Forty-five cases of combined neurofibromatosis and pheochromocytoma were collected from the literature. The syptomatology of pheochromocytoma is not changed by the combined occurrence with neurofibromatosis. The prognosis, as a rule, depends on the pheochromocytoma.

Open Lung Biopsy for Diffuse Pulmonary Lesions. L. J. Grant and S. A. Trivedi. Brit. M. J. 1:17-21 (Jan. 2) 1960 [London].

A series of 26 biopsies of the lung by thoracotomy is presented, general anesthesia being employed in all cases. The site of the incision was planned according to the maximal radiologic distribution of the pulmonary lesions. In earlier cases a routine thoracotomy incision was used, with or without removing a rib. In later cases it was found that a small anterolateral incision, usually about 6 to 8 in. (15 to 20 cm.) long, could be employed, with the possibility of extending it if desirable. The chest was opened through the rib bed without removing a rib; the lung was inspected and palpated, together with hilar and mediastinal lymph nodes; and a suitable node was removed for histological section. A portion of the lung, approximately 2 by 3 by 5 cm., showing most disease, was excised between 2 clamps. The lung was sutured in 2 layers by means of deep mattress and of superficial continuous chromic absorbable (catgut) sutures. After the insertion of antibiotics, the chest incision was closed, an intercostal drain being left for 24 to 28 hours.

There was no operative mortality in this series. In the majority of the patients there were no complications, the postoperative course being satisfactory. Only 2 patients developed minimal pyrexia, and one had a small pleural effusion which needed aspiration 3 days after removing the tube. In only 2 cases were the complications more serious. One patient, suffering from a honeycomb lung due to eosinophilic granuloma, developed a spontaneous pneumothorax on the contralateral side on the third postoperative day. The other patient developed a subacute intestinal obstruction on the 17th postoperative day, which responded well to conservative treatment. Histological findings were indefinite in 2 cases only; in one of these, however, they were sufficient to make the preoperative diagnosis improbable. In the remaining 24 patients the histological diagnosis was made, but in about one-quarter of them the etiology remained obscure.

Rupture of the Heart in Myocardial Infarction: Clinical and Pathologic Observations. L. H. Sigler. Am. J. Cardiol. 5:14-23 (Jan.) 1960 [New York].

The author reports on 5 women, between the ages of 56 and 76 years, and on 3 men, between the ages of 47 and 71 years, with myocardial infarction, in whom cardiac rupture was observed at the Adelphi Hospital in Brooklyn, N. Y. A review of the literature revealed an incidence of rupture of the heart, ranging from 7.11 to 10.5% among patients with myocardial infarction. The condition, however, appears to occur more often than the literature would indicate. The 8 patients died, and autopsy was performed on all. It revealed that cardiac rupture affected an area of the heart in which fresh myocardial damage was present, but never an area of organized infarction. In most of the patients it occurred in the free wall of the left ventricle, mainly in the anterolateral region close to the apex. It may involve portions of the lower interventricular septum, in occasional cases it may affect the interventricular septum alone, and rarely it may be confined to the papillary muscle.

The mechanism of rupture of the heart in patients with myocardial infarction is not fully understood. The pathological and clinical findings in the 8 patients and in those reported on by other workers suggest that several factors participate, such as preexisting and coexisting hypertension with its strain on the heart; hypertrophy of the myocardial fibers; the female sex in whom hypertension is more frequent; the older age groups in which the normal histological structure of the myocardium is altered; an early age of the infarct; the effect of leukocytic infiltration with its local enzymatic destructive effect on the myocardium; and the location of the coronary occlusion usually in the anterior descending branch of the left coronary artery. The most important direct cause appears to be an aneurysmal-like expansion of the devitalized myocardium in the area of infarction during systole, which produces a suction effect on the blood in that area. This probably causes overdistention and rupture of the arterioluminal and arteriosinusoidal vessels with dissection of blood through the myocardium. Pressure exerted by contraction of the adjacent normal heart muscle on the devitalized area also causes tearing of the diseased myocardial tissue.

Because rupture of the heart is rapidly fatal, recognition of its possible occurrence should be attempted before it happens. The diagnosis of rupture of the free wall of the heart during life is hard to make, but in perforation of the interventricular septum the diagnosis is relatively easy to establish. Treatment of the condition when affecting the free wall should, therefore, be prophylactic. The condition must be borne in mind in any case of myocardial infarction, especially when there is preexisting and coexisting hypertension, in the older age group and in women. Careful management of the acute phase of infarction is to be instituted. In perforation of the interventricular septum, treatment should be symptomatic and directed toward heart failure.

Presence of a Tumor Inhibitory Principle in Livers. P. A. Herbut and W. H. Kraemer. Am. J. Path. 36:105-111 (Jan.) 1960 [Ann Arbor, Mich.].

In earlier studies the authors had established the presence of a tumor inhibiting principle in the serum of some animal species. In this paper they describe tests on the tumor inhibitory activity against Gardner lymphosarcoma 6C$_3$HED of extracts of livers of several species of animals. The Gardner lymphosarcoma 6C$_3$HED was carried subcutaneously by C$_3$H mice, and the liver extracts were prepared with isotonic sodium chloride solution. Complete regression of growth was obtained with extract of guinea pig liver; marked but incomplete retardation of growth was induced by extracts of sheep, hog, and rabbit livers; slight and inconsistent retardation was demonstrated with extracts of horse and bovine livers; and no retardation was shown with extracts of 2 human livers. Electrophoretic patterns of each of the extracts showed little or no albumin and an abundance of globulin. It is thought that the differences in results obtained with the liver extracts of the various animal species may be due to limitation of dosage and perhaps to age of the host supplying the liver. These factors are now being investigated.

Cytodiagnosis of Generalized Cytomegalic Inclusion Disease Made in Patients During Life. M. De Groodt and M. Sebruyns. Rev. franç. étud. clin. et biol. 4:996-1001 (Dec.) 1959 (In French) [Paris].

The authors describe in detail the laboratory technique used in the Institute of Histology of the University in Ghent, Belgium, for the detection of cytomegalic inclusion bodies in the urine, the saliva produced by the parotid gland, and the gastric juice obtained from children with the clinical aspect of generalized cytomegalic inclusion disease. With the aid of Heidenhain's iron hematoxylin stain, the nuclear inclusions showed a dark blue to black color. Since hematoxylin is a basic stain, it may follow that the nuclear inclusions are basophilic, while other workers have described them as acidophilic. The fact should be emphasized, however, that acidophilia or basophilia is no specific property of the nuclear inclusions, the affinity of which for acid or basic dyes rather depends on the pH of the iron solution used.

The authors insist on the great diagnostic difficulties in the identification of cytomegalic-cell elements. They caution against the results of examinations of organic fluids performed in laboratories located at a great distance from the place where the patient sojourns, because the examination must be performed on fresh specimens. Furthermore, a close collaboration between the hospital and the laboratory is indispensable in order to succeed in the attempt of detecting a pathological entity which is still as ill-defined as the cytomegalic inclusion disease, and to reach a more accurate concept of its legitimate place in the classification of diseases.

Acute Necrotizing Glomerulitis: The Clinical Features and Pathology in Nine Cases. D. Bialestock and J. D. Tange. Australasian Ann. Med. 8:281-289 (Nov.) 1959 [Sydney, Australia].

The authors report on 9 patients with glomerular necrosis which led to oliguria or anuria, and to death in uremia. In 4 patients the glomerular lesion was associated with pulmonary hemorrhage. None was hypertensive; none had edema. These 4 patients suffered from terminal oliguria or anuria, and 2 also had hematuria. The signs of renal involvement appeared 10 days, 2 weeks, 7 weeks, and 7 months, respectively, after the onset of the pulmonary lesions. The duration of the illness in the remaining 5 patients varied between 1 and 4 weeks. The onset of the glomerular lesion was marked by vomiting and oliguria, progressing to anuria in 3 patients (one also had hematuria). Painless hematuria was the first symptom in the 4th patient and was followed 3 weeks later by anuria. The 5th patient was hospitalized with a respiratory infection and died the following day.

The kidneys of the 9 patients were comparatively normal in size, although swollen and showing points of hemorrhage throughout the cortex. On microscopic examination the glomeruli appeared damaged, with varying degrees of necrosis. The striking feature was the replacement of the whole, or the greater portion, of the tuft by deeply eosinophilic, amorphous material containing a small number of pyknotic nuclei and arranged in contiguous or confluent masses. Except for pulmonary hemorrhage in some patients, there were no lesions in other organs. The pathological process in this study shows affinities to both proliferative glomerulonephritis and polyarteritis nodosa, but its exact nature remains to be determined.

Clinical and Histomorphologic Considerations in 230 Patients with Mammary Secretion. U. Veronesi, R. Bianco and F. Bellini. Tumori 45:751-782 (Nov.-Dec.) 1959 (In Italian) [Milan, Italy].

The cases of 230 patients with mammary secretion observed at the Cancer Institute of Milan from 1928 to 1958 are reported. In 96 of the 230 patients the secretion was due to mammary carcinoma, in 58 to fibrocystic mastopathy, in 33 to papillomatosis, and in 25 to various other conditions. No histological examination was made in 18 cases. One hundred eighty-seven patients (81%) presented sanguineous secretion; 37 (16%), serous secretion; and 6 (3%), other types of secretion. The sanguineous secretion was found more frequently in patients with carcinoma (97%) than in those with papillomatosis (76%) or fibrocystic mastopathy (67%). A palpable mass was present in the mammary gland of 145 patients; 85 patients presented no palpable mass. Exploratory operation revealed a carcinoma, mainly intraductal, in 17 patients. Comparing the data obtained from this study with those on 4,675 patients with carcinoma, fibrocystic mastopathy, or ductal papillomatosis observed at the Cancer Institute of Milan during the past 30 years, the authors point out that mammary secretion is a rare symptom among patients with mammary carcinoma (96 out of 4,000 cases, or 2.4%), is less rare among patients with fibrocystic mastopathy (56 out of 605 cases, or (9.6%), and is very frequent among patients with ductal papillomatosis (33 out of 70 cases, or 47%).

Experimental Silicosis: The Inhibitory Effect of Iron. P. Gross, M. L. Westrick and J. M. McNerney. Dis. Chest 37:35-41 (Jan.) 1960 [Chicago].

Silicosis was induced in rats and guinea pigs by iron-contaminated silica. One group of rats was injected intratracheally with 1 cc. of quartz dust containing 8 to 9% iron; another group was injected with iron-free quartz. Some animals died immediately or within 24 hours; others died at various times from intercurrent diseases. Pairs of animals were killed for sampling at various intervals up to 16 months after the injection. Guinea pigs were exposed to the iron-contaminated quartz dust in an inhalation chamber for 6 hours a day, 5 days a week, during one year, under a dust concentration which averaged 44 mg. per cubic meter. Animals were killed at various intervals for sampling. The lungs of all the animals were inflated with Formalin at a pressure of 10 cm. of water, and paraffin sections were prepared for microscopic study.

Iron was found closely associated with silica in rats' lungs during the initial period after the injection. Three months later the lungs contained scattered cellular aggregates or small nodules, with no indication of collagen formation. The nodules varied in color and had a small content of iron, together with a high content of silica, showing the dissociation of the 2 substances. Nodules found in the rats injected with iron-free silica at one month were of the same size or larger than those found 3 or 4 months after the injection in the rats injected with iron-contaminated silica. At 6 months after the injection the nodules in the control animals showed a moderate collagen content, while those in rats injected with iron-contaminated silica contained little or no collagen. The essential difference between the 2 groups at 11-to-16-month intervals was that the control group had a greater number of nodules and larger masses of confluent nodulations than the experimental group.

In the guinea pigs not only the collagenization of nodules was inhibited, as in the rats, but also the formation of silicotic nodules was prevented by the contaminating iron. Although the iron had disappeared from regions where collagen had developed, there were other foci in which a manifest inhibition of collagen formation had taken place, in spite of the presence of abundant iron-free silica in those regions. This apparent inhibition of fibrosis in the absence of iron contradicts Gardner's premise (applied to aluminum) that the inhibiting substance, to be effective, must occupy the same cell as the quartz particle which it inhibits.

The Production of Fat Embolism in Rabbits by Feeding High Fat Meals. R. L. Swank, W. Blinsman and P. Sloop. Surg. Gynec. & Obst. 110:9-13 (Jan.) 1960 [Chicago].

The effects of fat accumulation in the vascular system as related to nutritional conditions were studied on 82 rabbits, of which 66 were fed cream and 16 were fed vegetable oil by stomach intubation. The dose of fat or oil ranged from 0.5 to 8 Gm. per kilogram of body weight, the largest feeding containing a lipid concentration of 36%. Electrocardiographic and electroencephalographic data, lipid, lipoprotein, and blood urea nitrogen determinations, and recordings of pathological changes in the tissues were obtained after the feeding. Death occurred in 43% of the animals that received 6.5 Gm. and in 57% of those that received 8 Gm. of cream or oil per kilogram of body weight. The period between the feeding and death varied between 20 and 34 hours, during which the animals became quiet and progressively weaker, with subsequent cyanosis, dyspnea, stupor, and, in some cases, convulsion.

Electroencephalograms and electrocardiograms were obtained for 30 rabbits which had received cream and for 4 which had received safflower oil.

Important electroencephalographic changes were observed in 9 of the 16 animals that were fed 8 Gm., in 1 of the 14 that were fed 2 Gm., and in 1 of the 4 that were fed 0.5 Gm. of fat per kilogram of body weight. The 4 rabbits that were fed safflower oil had a normal electroencephalogram. The electrocardiogram was abnormal in 8 of the 16 rabbits fed 8 Gm., in 3 of the 6 fed 4 Gm., in 4 of the 8 fed 2 Gm., and in 1 of the 4 fed 0.5 Gm. of fat or oil per kilogram of body weight.

Electrophoretic studies showed that lipoprotein values had increased considerably 24 hours after the fat feeding. Microscopic fat globules were demonstrated by dark-field illumination in the urine from a number of rabbits. The blood urea nitrogen value reached 30 mg. per 100 cc. in 4 of the 8 animals for which this determination was made. Fat emboli were demonstrated intravascularly, with multiple emboli observed as early as 6 hours, and as long as 96 hours, after the feeding. Visible pulmonary emboli were most numerous after the tube feeding of 2 and 4 Gm. of lipid per kilogram of body weight, and were least numerous after the feeding of 6.5 and 8 Gm. Fatty infiltration of the liver was observed in only 3 animals, and fatty degeneration of the heart muscles in 8.

The authors' interpretation is that fat emboli are a critical factor in slowing down the circulation only after larger fat meals, in excess of 4 Gm. of lipid per kilogram of body weight. This circulatory disturbance is due to hypoxia of the tissues. The filtering capacity of the capillaries is exceeded, and the fat emboli penetrate the general circulation, resulting in shock from multiple microembolism of the brain, lungs, and heart.

RADIOLOGY

Recurrent Seminoma: The Management of Late Metastasis, Recurrence, or a Second Primary Tumor. M. Friedman and M. C. Purkayastha. Am. J. Roentgenol. 83:25-42 (Jan.) 1960 [Springfield, Ill.]

The authors report on 24 patients who were treated during the past 14 years for recurrent seminoma of the testis. Recurrence of the tumor in these patients occurred several months or years after the initial surgical and irradiation treatment had been completed. Results of the studies of failure in this series prompted the authors to revise and amplify the technique of treatment in patients with seminoma of the testis, the proper application of which should result in a 5-year arrest rate exceeding 90%.

Survey of the results of this study showed that prognosis for recurrent seminomas is highly favorable. Of 18 patients in this series who were treated and who survived for 5 years after the first recurrence, the condition was arrested in 10; of 14 patients who were treated and who survived for 10 years after the first recurrence, the condition was arrested in 7. Of 20 patients who were treated and who survived for 5 years after orchiectomy, the condition was arrested in 14; of 17 patients who were treated and who survived for 10 years after orchiectomy, the condition was arrested in 9. When the metastasis, the recurrence, or the second primary tumor was the only late manifestation, the prognosis was excellent (7 of 10 patients survived 5 years); when it was the first of many recurrences, only 3 of 8 patients survived for 5 years. Arrest of the disease has been achieved in 3 of 9 patients with late metastasis to the left supraclavicular lymph nodes. When an apparently pure seminoma metastasizes to a supraclavicular lymph node, a larger irradiation dose is required but needs not exceed 2,000 r; an irradiation dose of 3,000 r is sufficient if the tumor is more malignant.

The treatment of 3 of 4 patients with late mediastinal metastasis, who received irradiation doses of about 3,000 r in 3 weeks, resulted in a survival of from 7 to 11 years. Arrest of the disease for more than 3 years was achieved in 2 of 4 patients who were irradiated for late lymph node metastasis occurring in the previously unirradiated retroperitoneal region. The remaining 2 patients died but might have been saved if irradiation had been given immediately after orchiectomy. Results of treatment in 5 patients with bilateral primary tumors of the testis, of whom 4 are living and well, show that the same general principles of treatment should be applied to the retroperitoneal lymph nodes of the second tumor as were used for the first, unless one is hindered by sequelae from treatment of the first tumor. If the second tumor is not seminomatous, a radical resection of the retroperitoneal lymph nodes on the side of the second tumor is mandatory, because the irradiation effects from the first course of treatment prevent administration of the larger tumor dose required. One of 6 patients in this series, who was irradiated with doses ranging from 2,500 to 2,900 r in about 2 weeks for metastases to the right scapula and to the left supraclavicular lymph node and to the upper left humerus, is alive and well 14 years after the last bone metastasis occurred.

Prolonged palliation and even an occasional cure are possible in patients with pulmonary metastasis from seminoma. Since they tend to be more aggressive and slightly more radioresistant, a tumor dose of 2,400 r in 3 weeks is recommended. Two patients in this series had recurrences in the base of the scrotum and were successfully irradiated. None of 4 patients who had remote generalized metastasis survived 5 years after the appearance of the first metastasis. Improper uses of irradiation techniques, such as inadequate tumor dose, failure to irradiate the next echelon of lymph nodes beyond the site of known disease, and improper placement of treatment portals, often are a cause for failure in the treatment of seminoma and result in recurrences.

BOOK REVIEWS

Neurology. By Roy R. Grinker, M.D., Director of Institute for Psychosomatic and Psychiatric Research and Training, Chicago, Paul C. Bucy, M.D., Professor of Surgery, Northwestern University School of Medicine, Chicago, and Adolph L. Sahs, M.D., Professor and Head of Department of Neurology, State University of Iowa, Iowa City. Fifth edition. Cloth. $24.50. Pp. 1386, with 445 illustrations. Charles C Thomas, Publisher, 301-327 E. Lawrence Ave., Springfield, Ill.; Blackwell Scientific Publications, Ltd., 24-25 Broad St., Oxford, England; Ryerson Press, 299 Queen St., W., Toronto 2B, Canada, 1959.

This new edition of a well-known American textbook is a vast improvement over the previous edition (1949). The third author has added the indelible imprint of his meticulous care and sound judgment. The book has been thoroughly revised and expanded to include the important advances in neurology in the intervening years and has been reorganized in keeping with those advances. In the preface the authors acknowledge the advice and consultative help of a large number of authorities who, in a variety of special fields, have served to make the text authoritative.

The volume opens with a chapter on the neurological examination of the patient which, for succinctness and coverage, is exemplary. It includes discussions on taking the neurological history; clinical examination, both mental and physical, of alert adults as well as of children and comatose and elderly patients; a description of special procedures, such as the withdrawal and examination of cerebrospinal fluid; x-ray studies, including pneumography, myelography, angiography, electroencephalography, and electromyography; and psychological testing. A new chapter on neurochemistry and metabolic diseases contains the bulk of what the clinician needs to know in this new and growing area. Gathered together here is information about the increasing numbers of disorders, some known formerly as degenerative diseases, for which metabolic disturbances are now known to be responsible. No doubt many more will be so reclassified in the future. Many somewhat uncommon but important disorders are described which were briefly mentioned or omitted from the earlier editions, such as phenylketonuria, galactosemia, and the lipidoses in their common subdivisions. The chapter on developmental defects is much fuller and more rationally constructed than in the previous edition.

The many standard neurological diseases are amply discussed in the succeeding chapters, yet with economy of space and words. A final section on neurological manifestations of certain medical diseases is a welcome addition, included in recognition of the importance to the neurologist and especially to the consultant neurologist, of such conditions as the collagen diseases in their varied types, hemopoietic disturbances, hepatic disease, hemochromatosis, and such diseases of the bone as osteitis and fibrous dysplasia. This chapter might be enlarged to include other important neurological complications of a host of basically non-neurological diseases. One regret is that drugs in this book are usually mentioned by their trade names; where possible, generic terms should be used. The bibliography at the end of the book lists about 3,000 references and contains little padding. The index is adequate.

This new edition earns high praise. It is the best American neurological text, going far beyond the briefer books so useful to students before examination, and is adapted to the needs of the serious neurologist. It approaches the definitive without attempting the encyclopedic presentation of the minutiae to be found in monographs on special topics. It sets forth the broad outlines of current neurological knowledge, and its attitudes reveal a satisfying soundness of judgment. There is nothing radical or quixotic here; no pet theories are promulgated, but always, so far as generous sampling indicates, a sane adherence to the demonstrated and factual is shown. Its errors are few and minor; those that the future may disclose will prove to be the errors of today's neurology and not those of a biased approach or of special pleading.

This appraisal may be documented by a few illustrative examples. The discussion of epilepsy is excellent, orthodox, and reliable, with a fair estimate but no worship of the electroencephalogram; rather there is an appreciation of the indispensable value of all our knowledge in this difficult field. The whole long discussion of cerebrosvascular disorders is informative and sound, with a shrewd therapeutic conservatism, including adherence to rigid criteria for surgical intervention, about which so much nonsense is practiced today in certain quarters. The same can be said for the discussion of craniocerebral trauma and its treatment. This edition, when compared with the previous one, is a revelation of the advances made in clinical neurology in the past decade. The neurologist can congratulate himself on this progress and on having seen his "queen of specialties" become an active discipline, dynamic in its outlook and promising new conquests in the future.

Roland P. Mackay, M.D.

Sociological Studies of Health and Sickness: A Source Book for the Health Professions. Edited by Dorrian Apple, Ph.D., Assistant Professor of Sociology, Boston University, Boston. Cloth. $7.50 Pp. 350. Blakiston Division, McGraw Hill Book Company, Inc., 330 W. 42nd St., New York 36; 95 Farringdon St., London, E. C. 4, England; 253 Spadina Rd., Toronto 4, Canada, 1960.

This book is described as a source book for the health professions. The studies in this volume were carried out by sociologists, anthropologists, and psychologists, partly in collaboration with physicians. The recognition of need for health care seems related to socioeconomic level for symptoms such as continued coughing or swelling of the ankles. More people from higher social levels said that the condition warranted seeing a physician. In poliomyelitis vaccine trials a markedly greater proportion of mothers from the lowest socioeconomic level refused permission for their child to be vaccinated. In such primitive settings as the Mestizo communities of coastal Peru and Chile, scientific medicine was not replacing folk medicine but was supplementing it.

There is an interesting chapter on health needs and opinions of older adults in a low socioeconomic district of Boston. The chapter on the psychological meaning of mental illness in a family is important as it reveals that there are many supports in society for maintaining a picture of normality concerning, for instance, a husband's behavior. Social pressures and expectations not only keep behavior in line but also, to great extent, perceptions of behavior. This suggests problems as yet unsolved. One study group was impressed by the more frequent problems of treated psychoneuroses in the higher social classes and of chronic schizophrenia in the lower classes. Patients in the mental institution are interesting material for a study of adjustment. Passivity seems to be the problem. Their health becomes the concern of physicians, nurses, and attendants and not their own responsibility. Organizations like the army, orphanage, prison, and hospital have in common the fact that they provide for their members a home away from home, relieving them of the burden of making decisions 24 hours a day. One writer states, "When the patient returns to civilian life, his suddenly uncorseted soul seems flabby and incapable of standing alone."

Alcoholism is discussed in detail. One of the conclusions is that high rates of alcohol consumption do not necessarily mean high rates of alcoholism. There is a good explanation of the accepted fact that the Irish have the highest rate of alcoholism and the Jews have the lowest rate. This fact, however, cannot be used to show that Jews are less subject to compulsive behavior as, in a World War I study, they were found to have a higher rate of drug addiction than any other ethnic group.

A hospital has one of the most complex social organizations of any place of work in our society. There is formal and informal organization, and either can retard changes in the other. In every organization there are some official regulations which by tacit consent are never carried out. These studies show, however, the importance of group interaction and how it results in care of the patient. Interestingly, it is assumed somewhat irrationally that because one works in a hospital one somehow acquires knowledge about health and disease. Neighbors will confer with such a person about their symptoms.

This book provides an interesting reference for physicians who wish to learn about the thinking of other members of the health team. Studies included seem objective and well documented with statistical evidence. It is important for the physician, as captain of the health team, to recognize that there are at least 80 allied health professions and services with direct interest in the patient.

Franklin Yoder, M.D.

The Treatment of Bronchial Neoplasms. By Robert R. Shaw, M.D., and Donald L. Paulson, M.D. With chapter on Bronchial Adenoma by John Lester Kee, Jr., M.D. Publication number III, John Alexander monograph series on various phases of thoracic surgery, memorial to John Alexander (1891-1954), Professor of Surgery, University of Michigan. Editor: John D. Steele, M.D. Editorial Board: Howard T. Barkley, M.D., and others. Cloth. $8. Pp. 135, with illustrations. Charles C Thomas, Publisher, 301-327 E. Lawrence Ave., Springfield, Ill.; Blackwell Scientific Publications, Ltd., 24-25 Broad St., Oxford, England; Ryerson Press, 299 Queen St., W., Toronto 2B, Canada, 1959.

The authors of this monograph are a group of thoracic surgeons who have been the major contributors to the development of surgical techniques for resection and suture of the bronchus without necessitating removal of the distal lung tissue. These bronchoplastic procedures used in the treatment of traumatic injuries to the bronchus and in bronchial stenosis have been dramatic in the preservation of lung tissue and, in many instances, life. Interest in the book centers around the application of these procedures in the treatment of bronchial neoplasms. Material for this work is drawn from the surgical practice of the group. Treatment is presented in its entirety, including surgery, radiation therapy, chemotherapy, and terminal care of the cancer patient. From this broad approach the relative role of bronchoplastic procedures is apparent. It is the surgeon's concern for the comfort and quality of survival of his patients that gives these techniques significance in the treatment of cancer. This art of using knowledge and skills, within the framework of their limitations, for the service of individual patients is well expressed in this book.

It is interesting to observe the reactions of the surgeon as a scientist treating disease. Here, in relation to tumors of the bronchus, is echoed a dissatisfaction in the accomplishments of early diagnosis and radical operations in significantly altering the survived statistics of a group of cancer patients. This feeling, prevalent throughout the medical world, arises in spite of the proved usefulness of these methods. It has led to the adoption of other theories and philosophies of cancer growth. The authors express these as the temporal theory, predeterminism, and the biological nature of tumors. Some effort is made to demonstrate these theories by case reference, but it is apparent that these concepts are as yet poorly substantiated by quantitative observations. They exist, along with the concern with the quality of patient survival and a pride in small differences in mortality and survival statistics, as a necessary stimulus for continued efforts to overcome the disappointment in the present treatment of neoplastic disease.

For anyone interested in these subjects, the book is worth reading. Due to its lack of historical perspective and presentation of an extensive review of the literature in the form of a bibliography, it falls short of being considered a monograph. Except for the reiteration of philosophy and an expression of attitudes, the book might be condensed to the last 30 pages, which exist as an excellent paper on the subject.

JEROME R. HEAD, M.D.

Histologie und mikroskopische Anatomie des Menschen. Von Dr. W. Bargmann, o.ö. Professor der Anatomie an der Universität Kiel. Third edition. Cloth. 69.60 marks; $16.55. Pp. 820, with 658 illustrations. Georg Thieme Verlag, Herdweg 63, (14a) Stuttgart, West Germany [Intercontinental Medical Book Corporation, 381 Fourth Ave., New York 16], 1959.

This edition of a well-known German textbook of histology retains the familiar format of the previous edition. Principal changes from the earlier volume are in those areas in which electron microscopy has contributed much to current knowledge of cell and tissue morphology and function; as a consequence of this aspect of present-day biological research, those sections have been revised extensively. Many new illustrations, chiefly electron micrographs and diagrams derived from electron microscope studies, have been added. The text has been revised to include discussion and comment on these pertinent findings. Examples of the newer material include illustrations of the ultrastructure of peripheral myelinated nerve fibers, nonmyelinated nerve fibers, nodes of Ranvier, synapses, thrombocytes, lung capillaries, sperm cells, skin, mammary gland, retinal rod cells, and crista ampullaris.

As do previous editions, this volume stresses the significance of morphology not in the static descriptive sense but in its relation to function as a coequal partner in physiological, biochemical, and clinical dynamics. It is a textbook of normal histology designed for students of medicine and graduate students in biology, and as such it is well-written and illustrated and accomplishes the synthesis of the biological and clinical disciplines in a superb way.

Illustrations include photomicrographs, drawings, and schematic diagrams which are remarkable for their clarity. The 24 illustrations in color are those from the previous edition. Literature citations have been expanded to include selected references current as of 1959. An excellent table of contents and an index are provided. The type is clear and easy to read, and the binding is sturdy and attractive. This book can be recommended to medical students, pathologists, and graduate students in the various biological sciences as an excellent textbook and reference book of human histology and microscopic anatomy.

Handbook of Physiology: A Critical, Comprehensive Presentation of Physiological Knowledge and Concepts. Section 1: Neurophysiology. Volume II. Editor-in-chief: John Field. Section editor: H. W. Magoun. Executive editor: Victor E. Hall. Cloth. $20. Pp. 781-1439, with illustrations. Distributed for American Physiological Society by Williams & Wilkins Company, 428 E. Preston St., Baltimore 2, 1960.

In this handbook, the society proposes to provide a comprehensive and critical presentation of the state of knowledge in the various fields of physiology. It intends to cover the physiological sciences in their entirety once in 10 years in a critical, comprehensive survey of physiological knowledge and concepts, emphasizing each science according to its importance, regardless of the time when the discoveries and formulations were made. Section 1 is devoted to neurophysiology, section 2 to circulation, and section 3 to respiration. Three volumes are to constitute the section on neurophysiology. Volume 1 appeared in 1959 and was concerned mainly with the historical development of neurophysiology, the initiation and transmission of nerve impulses, evoked potentials, sensory mechanisms, vestibular mechanisms, and the physiopathology of epileptic seizures. Volume 3 is in preparation.

Volume 2 considers the motor and the central regulatory mechanisms. These papers are addressed to persons with a broad background in physiology who need to increase their understanding and sophistication to that level adequate for predoctoral study for teaching and for preliminary orientation in preparation for research. This book succeeds admirably in fulfilling its aims. Each chapter is the effort of acknowledged experts. Half of the authors were selected from outside the United States so that the book is an international work. If the contribution was written in a language other than English, it has been competently translated.

It is not possible to single out chapters of this massive volume for comment. All are excellent. The editing is first-rate throughout the volume. There is a certain uniformity of presentation which is pleasing; each chapter is headed by an outline of chapter content which is followed by an introductory statement, a historical outline, and a thorough-going survey of the problem. Often the writer has made significant contributions to the subject. Frequently, a summary concludes the chapter. There is a full reference list for all but one chapter. There is an index of 17 pages. The book is beautifully printed. This authoritative volume is an indispensable reference for persons engaged in teaching or research in the field of neurology and related disciplines. The maintained quality of presentation from chapter to chapter is a pleasure to behold. The authors deserve commendations; even more so do the editors who chose them and who fitted the pieces gracefully together into an outstanding work of reference.

Charles D. Aring, M.D.

Aldosterone in Clinical and Experimental Medicine. By E. J. Ross, M.D., Ph.D., M.R.C.P. Senior Lecturer in Medicine, University College Hospital Medical School, London. Cloth. $5.50. Pp. 144. Charles C Thomas, Publisher, 301-327 E. Lawrence Ave., Springfield, Ill.; Blackwell Scientific Publications, Ltd., 24-25 Broad St., Oxford, England; Ryerson Press, 299 Queen St., W., Toronto 2B, Canada, 1959.

The subject matter of this book is well organized and presented in a concise manner. The book should be helpful to the investigator and the practicing physician. The references are excellent, and unnecessary detail is absent. Only pertinent data and facts which have proved to be practical are presented. The comparison of animal data with those of normal human subjects is excellent. The correlation between certain observations in patients with various diseases and that between those in normal human beings is presented in simplified form. This book is an excellent one on a new subject and should be of interest to the clinician as well as to the experimental investigator.

Harley E. Cluxton Jr., M.D.

Diagnosis and Treatment of Tumors of the Chest. Sponsored by American College of Chest Physicians. Editorial Board: David M. Spain, M.D., chairman, editor-in-chief, and others. Cloth, $14.75. Pp. 371, with illustrations. Grune & Stratton, Inc., 381 Park Ave. S., New York 16; 15/16 Queen St., Mayfair, London, W. 1, England, 1960.

Due to the continually increasing knowledge of various tumors of the chest, this volume is especially timely and has been prepared by an outstanding, internationally known group of contributors. Primary tumors of all of the intrathoracic organs, as well as of the chest wall, diaphragm, and pleura, are described, and metastatic tumors of the lung and the management of inoperable primary tumors of the chest are discussed. All modern methods of diagnosis of these lesions, including special x-ray techniques and bronchoscopic and cytological examinations, are dealt with in an erudite manner and are well illustrated. Therapeutic measures, including surgery and irradiation, and the advanced thinking which goes into treatment are presented and discussed.

In the case of bronchogenic carcinoma, discussion of etiological factors and experimental production of these lesions add materially to the scope of their understanding. Etiology, pathogenesis, pathology, diagnosis, and treatment are thoroughly covered and add materially to the teaching value of this work. High-quality illustrative material has been selected wisely and used generously throughout the book. Angiocardiography is ably discussed in the section on tumors of the cardiovascular system. The subject matter is thoroughly treated in a clear, concise, and understandable manner. The volume has adequate references and is well documented with clinical material. This timely volume should be of great value to all practicing physicians and surgeons in this field. It should also be a most useful textbook for graduate and undergraduate students.

William E. Adams, M.D.

Premature Babies: Their Nursing Care and Management. By A. K. Geddes, M.D., Associate Professor Pediatrics, McGill University, Montreal, Canada. Cloth. $4.50. Pp. 215, with 13 illustrations. W. B. Saunders Company, 218 W. Washington Sq., Philadelphia 5; 7 Grape St., Shaftesbury Ave., London, W. C. 2, England, 1960.

This book on the care of premature and immature infants was written as a textbook or reference book for nurses. It is brief and well organized but repetitious. The author defends this point in the preface by explaining that the repetition was "to promote clarity and obtain emphasis." His style of writing is clear, and he avoids complicated medical terms. This promotes interesting and easy reading. The author does not discuss some of the important instructions to the nurse. He devotes many pages to listing material and equipment necessary in a nursery for premature infants but omits the mention of good records and charting of information on each infant, which would be most helpful to the attending physician in treatment. The type of resuscitation which he has outlined does not conform with present standards. The author passes lightly over feeding techniques, and I do not agree with his recommendation of formulas.

The discussion of the most common reflexes in the premature infant does not include an explanation of the tonic-neck reflex and reciprocal motion, which are important diagnostic signs. Nowhere in the text does the author discuss means of transporting the premature infant from home to the hospital. I think he should have presented a chapter on preparing the mother to receive the graduate premature infant, with instructions and demonstrations on its feeding and care. Last but not least, this book would have been more valuable if the author had devoted space to the subject of possible infectious outbreaks in the nursery and what steps should be taken if an outbreak occurred. This book does not come up to current standards of a nurses' textbook or reference book on the care of the premature infant. Much important material has been omitted, and much has been discussed too briefly.

Herman N. Bundesen, M.D.

Drugs of Choice 1960-1961. Walter Modell, M.D., editor, Director, Clinical Pharmacology, and Associate Professor of Pharmacology, Cornell University Medical College, New York City. [Second edition.] Cloth. $13.50. Pp. 958, with illustrations. C. V. Mosby Company, 3207 Washington Blvd., St. Louis 3; Henry Kimpton, 134 Great Portland St., London, W. 1, England, 1960.

Making its appearance for the second time, after a two-year interval for revision, the 1960-1961 edition of this publication appears to be even more useful than the 1958-1959 volume. Several new chapters have been added, and three of the original chapters have been rewritten by new contributors. The outstanding feature of the book is the attention that is given to comparisons between drugs as a guide to proper selection and the choice of drugs to be preferred for a given purpose. Not all drugs are mentioned, either because some are too recent for objective comment or, in the case of older drugs, because they are not considered important. The new edition features an all-inclusive drug index (in place of the separate lists after each chapter in the first edition) which precedes the general subject index at the end. Thus, some drugs listed in the drug index are not mentioned in the text, whereas only drugs which are discussed or mentioned in the body of the book are included in the general index.

Although this highly practical publication provides rather sketchy information on some drugs, it should not be regarded as a short-cut to knowledge in this field. Indeed the book must be read thoughtfully to gain the evaluative viewpoint of the contributors. Accordingly, it is less desirable than standard textbooks on therapeutics for students, but it should appeal to the practicing physician as a reliable and fairly complete source of expert information on the selection of therapeutic agents.

H. D. Kautz, M.D.

A Textbook of General Physiology. By Hugh Davson, D.Sc. Second edition. Cloth. $14.50. Pp. 846, with 384 illustrations. Little, Brown & Company, 34 Beacon St., Boston 6; J. & A. Churchill, Ltd., 104 Gloucester Pl., Portman Sq., London, W. 1, England, 1959.

This second edition differs from the first (reviewed in *J. A. M. A.* 148:686 [Feb. 23] 1952) by the addition of nearly 100 figures and three chapters ("The Sensory Response," "Excitability of Cardiac Muscle," and "Electrical Activity in Smooth Muscle"). The pace of research in general physiology has been such that the author was obliged to consult nearly 2,500 additional original papers, reviews, and monographs; consequently, although the type is now smaller, the text has been increased by about 200 pages.

The purpose of the book is to study "those aspects of living material that show some immediate prospect of being described in terms of the known laws of physics and chemistry." The six major divisions are devoted to the structural basis of living matter, the transformations of energy in living systems, the transport of water and solutes, the characteristics of excitable tissue, the mechanism of contraction of muscle, and the relation of the organism to certain forms of radiation. The author apparently does not consider many physical aspects of living things, such as hardness, tensile strength, and response to mechanical vibrations of sonic and ultrasonic frequencies. If he does, neither the table of contents nor the index affords an easy clue to the location of these subjects in the text. The book is written for students and research workers in the basic sciences. From the standpoint of the medical reader its value lies principally, perhaps, in the wealth of magnificent illustrations, particularly electronmicrographs, and in the detailed consideration of molecular processes underlying cellular activity.

Frederic T. Jung, M.D.

Ocular Vertical Deviations and the Treatment of Nystagmus. By J. Ringland Anderson, M.C., M.D., B.S., F.R.C.S.Ed. With foreword by Sir Stewart Duke-Elder, G.C.V.O., M.D., D.Sc., LL.D. Second edition. Cloth. $8.50; 42 shillings. Pp. 189, with 60 illustrations. British Medical Association, B.M.A. House, Tavistock Sq., London, W. C. 1, England; [distributed in Western Hemisphere by] J. B. Lippincott Company, E. Washington Sq., Philadelphia 5; 4865 Western Ave., Montreal 6, Canada, [by arrangements made by its subsidiary, Medical Market Research, Inc., with British Medical Association], 1959.

No muscles in the body require more careful study, evaluation, and knowledge of coordination and intimate physiology than the eight eye muscles, particularly those involving the vertical movement of the eyes. Each patient requires individual and critical study which should not become mere routine.

The author has prepared a guide, particularly to vertical anomalies of the eyes, with the assessment of the probabilities of relief by orthoptics or surgery or both.

After analyzing the various and sometimes subtle components of vertical deviations such as fusion, fixation, abnormal vertical stimulation, and dissociated deviations in 600 concomitant and paralytic types of defects, he describes his methods of investigation, examination, and desirable choice of operation for each defect. His chapters on surgery of the oblique muscles should be used as a constant guide to the ophthalmic surgeon interested in obtaining not only a cosmetic but also a good, well balanced, functioning result. His chapter on nystagmus includes eccentric fixation and gaze nystagmus, the influence of conjugate deviation, and convergence. The nonsurgical and surgical treatment of nystagmus is entirely new and should be read by ophthalmologists interested in this perplexing problem.

Richard A. Perritt, M.D.

Experimental Surgery Including Surgical Physiology. By J. Markowitz, M.B.E., M.B., Ph.D., Professor of Physiology, University of Toronto, Toronto, J. Archibald, D.V.M., M.V.Sc., Dr.Med.Vet., Professor & Head of Division of Small Animal Medicine and Surgery, Ontario Veterinary College, Guelph, and H. G. Downie, D.V.M., M.S., M.V.Sc., Professor & Head, Department of Physiological Sciences, Ontario Veterinary College. Fourth edition. Cloth. $12.50. Pp. 931, with 580 illustrations. Williams & Wilkins Company, 428 E. Preston St., Baltimore 2, 1959.

This is a thoroughly revised and improved edition of a book long established as the primary reference for persons working in experimental surgery. It contains a wealth of material which can save the novice from repeating many common errors, and it indicates methods of proved value which can set an experimental project ahead by several months. Beginning with sections on the philosophy of the use of animals in medical research and their care and feeding, it progresses systematically through anesthesia and surgical technique, the problems of the alimentary tract, peritonitis, the pancreas, the biliary tract, the skeleton, the respiratory and circulatory systems, the urogenital system, and the central nervous system. Chapters are devoted to hypothermia, transplantation, and the visceral organism.

If there is any area which lacks adequate coverage, it is perhaps that of the germ-free animal. The entire work is enriched by numerous literary references, many of them best appreciated by the student of classics. The bibliographies at the ends of chapters are ample, and the index is useful and reasonably full. The book is highly recommended for students and practitioners of surgery and its specialties and for other persons engaged in surgical research, physiology, and experimental pathology.

Jonathan E. Rhoads, M.D.

Symposium on Emphysema and the "Chronic Bronchitis" Syndrome, Aspen, Colorado, June 13, 14, 15, 1958. Sponsored by Colorado Tuberculosis Association, Colorado Trudeau Society, University of Colorado School of Medicine, Colorado Foundation for Research in Tuberculosis, National Tuberculosis Association, American Trudeau Society. [Also published as Am. Rev. Respir. Dis., vol. 80, number 1, part 2, July 1959.] Cloth. Pp. 213, with 115 illustrations. [Colorado Foundation for Research in Tuberculosis, 4200 E. 9th Ave., Denver 20], 1959.

Pulmonary emphysema has been and remains a perplexing problem. One of the reasons for the perplexity surrounding the study of this disease has been the nomenclature associated with it. In the past all types of emphysema have been given various names by different authors so that at present confusion reigns in this area. This symposium has attempted to clarify the situation by delineating and defining the problem of primary chronic obstructive pulmonary emphysema, a single disease entity secondary to no other pulmonary disease. The problem is discussed from all viewpoints. Special reference is given to the research in this field. The course of events that leads to the full-blown picture is presented from the etiological, physiological, and pathological aspects. Only one paper concerns the therapy of pulmonary emphysema, and this paper appears to be one of the highlights of the conference. Each paper is followed by a transcript of the general discussion that took place after the presentation, a valuable part of the symposium. This book should be of interest to those who wish to obtain a bird's-eye view of pulmonary emphysema today, but it will give them little information regarding the management of such a problem in clinical practice.

Jerome R. Head, M.D.

Der Augenarzt. Band II. Herausgegeben von Karl Velhagen, Direktor der Klinik für Augenkrankheiten der Humboldt-Universität (Charité) Berlin. Mit Beiträgen von W. Comberg et al. Cloth. 122.30 marks. Pp. 901, with 435 illustrations. VEB Georg Thieme, Hainstrasse 17/19, Aufgang C, Leipzig C 1, East Germany, 1959.

This second volume of a major German textbook of ophthalmology is divided into 12 chapters dealing with methods of clinical examination and the required instruments, the light sense and its study with recently developed equipment, anomalies of refraction, aniseiconia, physiology and pathology of the pupil, x-ray diagnosis, clinical electroretinography, physical therapy, lacrimal apparatus, and the sclera. The numerous illustrations, many in color, are excellent. The bibliography is rather limited, as few American studies are cited. The organization of the material might have been improved. The book should, however, be welcomed as a highly useful reference work.

Ernst Schmerl, M.D.

Principles and Practice of Obstetric Anaesthesia. By J. Selwyn Crawford, M.B., Ch.B., D.A. Cloth. $4. Pp. 128. Charles C Thomas, Publisher, 301-327 E. Lawrence Ave., Springfield, Ill.; Blackwell Scientific Publications, Ltd., 24-25 Broad St., Oxford, England; Ryerson Press, 299 Queen St., W., Toronto 2B, Canada, 1959.

This small book is a critical evaluation of the methods of obstetric analgesia and anesthesia as currently practiced in Great Britain. It reviews the physiology of the mother as related to childbirth. There is an excellent discussion of the placenta and of placental transmission of respiratory gases, which are presented as a basis for the dissertation on analgesia in labor, general and regional anesthesia for delivery, and resuscitation of the newborn infant. Account has been taken throughout the book of the requirements of home delivery practice. This small book is well bound, and the type is easily legible. It is recommended for obstetricians and anesthesiologists.

Mary Karp, M.D.

QUESTIONS AND ANSWERS

BAROSINUSITIS

To the Editor:—*During an air flight from Montreal, Canada, to Boston on a hot and sunny summer day (90 F) a woman had a frightening experience. When the plane began to lose altitude preparatory to landing, she suffered a severe pain "at the hairline over the forehead." She described the pain as being intense for several minutes, improving slightly, becoming worse again, and finally decreasing to about one-half its intensity when the plane landed. The pain persisted at this intensity for about five hours and was practically gone after a night's rest, although there was a mild ache above the left eye and over the forehead. When the pain first started she thought she was going to die. In addition, she complained of a visual disturbance like a "blacking out" which soon disappeared. She pointed to the area of the left frontal sinus, particularly, but said that it seemed to go across the entire forehead and up to the hairline. She seemed none the worse for her experience 24 hours later. I would appreciate information regarding such an experience.*

M.D., Massachusetts.

Answer.—The symptoms described probably were due to a brief episode of barosinusitis, more especially in the left frontal sinus. The basic cause of this difficulty is the pressure differential between the air entrapped in the sinus and the ambient pressure of the atmosphere the patient is breathing. This can be expected to occur on descent of the aircraft preparatory to landing. The most common symptom accompanying barosinusitis is an extremely sharp pain or stinging sensation. The location of the pain depends on which sinuses are affected. Most frequently the frontal sinus will be involved, then the maxillary sinus. The pain is usually of sudden onset and severe intensity during descent. As a rule, the pain continues from the time of onset until the time of landing, but occasionally it persists or recurs for some hours or several days. A difference of pressure between the air contained within a sinus and that of the atmosphere will result if the sinus ostium is occluded by any developmental or acquired formation that acts as a valve and thus permits air flow through the ostium in one direction only. The most common contributing factor is the presence of upper respiratory infection.

CARDIAC PATIENTS AT HIGH ALTITUDES

To the Editor:—*What is the effect of altitude on a cardiac patient whose heart is kept well compensated by digitoxin? I have a patient who has spent his whole life in Arkansas at near sea level and wishes to vacation in Colorado at an altitude of 5,000 to 10,000 ft. for a week or two. He weighs 240 lb. at a height of 5 ft. 5 in. He has a moderate degree of pulmonary fibrosis, occasional runs of extrasystoles, and a mean blood pressure of 140/86 mm. Hg. Would such an excursion be harmful?*

M.D., Arkansas.

Answer.—Most cardiac patients can visit Colorado cities at an altitude of under 6,500 ft. without experiencing difficulties. Many notice from the beginning, and most after a week or two, no special difference. An occasional patient feels that he is definitely shorter of breath on very mild exertion. On the other hand, many believe they feel better—possibly because of other climatic factors or just because they are on vacation. It is probably unwise for cardiac patients to come from sea level directly to altitudes above 7,000 ft., although many do, feel well, and have no difficulties. In any case, and especially in going to altitudes above 7,000 ft., physical activity should be limited the first couple of weeks. Trips by automobile over passes 10,000 ft. high do not seem to present a problem, but staying overnight at high altitudes should be avoided until there has been some acclimatization.

ALTITUDE AND HEART DISEASE

To the Editor:—*I would appreciate information on the effect of high altitudes on cardiac patients. A patient has arteriosclerotic heart disease and complains only of dyspnea on moderate exertion. On one occasion he awoke during the night choking for breath. This episode cleared up in about one-half hour, without medication. The patient desires to move from this part of the country and to settle in Arizona (southern portion) or New Mexico. Is the altitude in these locations suitable for the type of patient described? If this happens to be the case in any specific locales, I should like to know of them even if they do not happen to be in the states mentioned.*

M.D., Illinois.

Answer.—The essential point in the problem of the case cited is not the effect of altitude but that of the treatment of this condition at any altitude. From the information given it seems certain that there is a markedly limited myocardial reserve,

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The answers here published have been prepared by competent authorities. They do not, however, represent the opinions of any medical or other organization unless specifically so stated in the reply. Anonymous communications cannot be answered. Every letter must contain the writer's name and address, but these will be omitted on request.

especially involving the left ventricle, provided the chief symptom is dyspnea and not substernal pain. It is of vital importance, therefore, to plan the life of the patient to avoid the strain of overactivity, nervous tension, and overeating. He is evidently good for but little under the circumstances and needs almost complete rest until he has recovered adequate reserve. Even more important is his need of digitalis. He should be digitalized conservatively, and the digitalization should be maintained thereafter by daily rations. He may take 1½ grains (0.1 Gm.) of old-strength digitalis three times a day for five to seven days, then 1½ grains daily thereafter, or he may take similar numbers of 1 grain (0.65 Gm.) doses of U.S.P. XI standard, which is 33 to 50% stronger than the old digitalis. If these measures are not effective in preventing any further failure, he should also receive diuretic therapy, preferably with mercurial agents at intervals. Life can be much prolonged and made more comfortable by the measures just cited, no matter what the altitude is, although it would be reasonable to advise that altitudes of 10,000 ft. or more be avoided and that effort in hilly country also be avoided at any altitude. If the measures of treatment outlined are carried out there is no particular reason why the patient should not settle in Arizona or New Mexico.

TRIP TO EUROPE FOR CARDIAC PATIENT?

To the Editor:—*A 67-year-old man had a severe coronary occlusion, with infarction, in January, which left him with a scar, some cardiac enlargement, blood pressure of 110/70 mm. Hg (prior to the thrombosis, 135/85 mm. Hg), and a significantly abnormal electrocardiogram. He has minor angina pectoris on exertion, excitement, or when exposed to cold weather, and, rarely, episodes of congestive heart failure with pulmonary edema, which subside after two or three hours. He is working at a desk job on a limited scale. Would it be too much of a risk for him to take a three-week trip to Europe in a pressurized plane, with a modest schedule that does not include much sightseeing?* *M.D., Washington, D. C.*

Answer.—It is hazardous to pass judgment on the ability of a patient, such as the one described, to withstand a three-week trip to Europe. Much depends on whether his trip will include episodes relating to business or other situations that will put him under excessive emotional or physical stress. Unfortunately, these cannot always be predicted in advance. A decision of this type depends somewhat on the philosophy of the patient. He should understand that he may develop congestive failure or acute myocardial infarction abroad, but that this might also occur at home. If the condition of the patient seems reasonably good and he desires to travel, on a limited scale, the decision should rest with him. He should be given instructions, however, on the steps he should take in the event of a change in his condition. Among the most helpful steps is to provide him with a list of reliable internists or cardiologists practicing in the main cities he plans to visit. This will insure his receiving good care if a complication should develop.

IMMUNIZATIONS BEFORE GOING TO EUROPE

To the Editor:—*What immunization do you consider necessary for a trip to Italy, France, England, and Germany? Would you advise a series of typhoid inoculations in a woman aged 55 years who had typhoid as a child? Also, is the intradermal method of typhoid immunization as good as the subcutaneous?* *M.D., New York.*

Answer.—For the trip proposed it is advisable to establish the absence of susceptibility to or to immunize against smallpox, typhoid, typhus, and diphtheria. Inoculations for immunization against typhoid should not be necessary for a person who has had the disease. Intracutaneous injections of typhoid vaccine will produce immunity, but it is generally believed that the subcutaneous route should be used. For a journey as extended as the one contemplated it seems advisable to be protected also against typhus.

DOSAGE OF VACCINES FOR CHILDREN

To the Editor:—*Since I have the responsibility of immunizing certain personnel for Asiatic travel, please answer the following queries: 1. What are the accepted dosages for children of the following vaccines and the minimal age limit for receiving such vaccines: typhoid-paratyphoid, cholera, typhus, tetanus, and plague? 2. In adults, how many separate vaccines are accepted as being safe to give at one time?* *M.D., California.*

Answer.—1. Children under one year of age are not often given typhoid-paratyphoid vaccine, but if there is good reason for doing so the total dose is 1 cc. of vaccine. Febrile reactions are common, however, and for that reason the total dose should be divided, the primary one not to exceed 0.2 cc. The second and third doses may each be 0.4 cc. if reaction to the first dose was not too severe. Children over one year of age should be given the adult dose of 1.5 cc., divided into three injections (0.3 cc., 0.5 cc., and 0.7 cc. respectively). For typhus vaccinations in children under the age of 6 years, two subcutaneous injections of about 0.25 cc. of vaccine have been suggested, at an interval of two to four weeks. For cholera, the total adult dose is 1.5 cc. The same plan as for typhoid-paratyphoid vaccine should be followed. If the child has not been immunized against diphtheria, tetanus, and pertussis it would be advisable to use the triple antigens in three doses of 0.5 cc. each, at intervals of four to six weeks. This immunization can be started as early as the 2nd or 3rd month of life. The total adult dose of plague vaccine is 1.5 cc. For children under one year of age one-fifth of the adult dose is recommended; for age 1 to 2 years, two-fifths; for age 5 to 10 years, three-fifths; and for age 11 years and over the full adult dose. It has been said that no severe reactions occur. The "International Quarantine Measures" recommend plague inoculations only during an epidemic.

2. The triple antigens (diphtheria, tetanus, and pertussis) are in common use and have caused few difficulties aside from a small number of instances attributed to the pertussis vaccine. Nevertheless, it is not wise to institute a number of other immunization procedures at the same time. Sharp reactions are always possible from typhoid vaccine, and severe local reactions may occur from smallpox vaccinations. If a number of inoculations are made simultaneously it may be impossible to tell whether one or the combination of antigens was responsible for a severe reaction.

PREVENTIVE INOCULATIONS FOR TROPICAL RESIDENCE

To the Editor:—*A former patient is planning to live for a time on the island of Trinidad. He has asked for advice about the necessary vaccinations, inoculations, and other preventive measures that might fortify him against certain tropical ailments. Would you please discuss this problem?*

M.D., New York.

Answer.—There are no tropical disorders peculiar to Trinidad that are not encountered in other tropical areas, and the specific preventives or vaccines needed for Trinidad are those necessary for any similar community.

A person going from a temperate climate to Trinidad should be vaccinated against typhoid, paratyphoid, smallpox, and diphtheria. There are no other specific measures that have been proved valuable or necessary. Malaria is the chief disease problem of the island, but there is no vaccine for this infection. There are no prophylactic drugs which will prevent an attack of malaria after a bite by an infected mosquito. Quinine and quinacrine hydrochloride will minimize the intensity of an infection or keep it at a subclinical level, but these drugs should be taken only according to the directions of the local physician or health officer. Persons should be advised to sleep in screened quarters or under mosquito nets and to avoid unnecessary exposure after dusk. There is no active yellow fever in Trinidad.

Other general measures, such as the use of light clothing, boiling of water, and avoidance of fresh fruits and vegetables, are necessary, as in any tropical area, and are covered completely in Stitt's chapter on tropical hygiene (Diagnosis, Prevention, and Treatment of Tropical Diseases, ed. 6, Philadelphia, Blakiston Company, 1956).

TYPHUS IMMUNIZATION FOR PAN AMERICAN HIGHWAY TRIP

To the Editor:—*Is it advisable to immunize a person who is going to Mexico, Central America, and South America along the Pan American highway against endemic typhus, epidemic typhus, or both?* *M.D., Illinois.*

Answer.—A person contemplating a trip to the areas mentioned in the query should be vaccinated against epidemic, or louse-borne, typhus. Vaccination against endemic, or murine, typhus is not considered necessary.

PRECAUTIONS ON TRIP TO AFRICA

To the Editor:—*Concerning immunizations for a trip through Kenya, Tanganyika, Mozambique, and South Africa, two drugs, chloroquine phosphate and quinacrine hydrochloride, were mentioned as preventing malaria. Atabrine has also been suggested. Which one would be best? Thirty years ago, when going to the Far East, one was told not to eat salads, berries, and uncooked vegetables. Would the same advice apply to Africa?* *M.D., New York.*

Answer.—Chloroquine diphosphate is preferred over quinacrine hydrochloride for the suppression of malaria. Atabrine is the commercial name for quinacrine. Single weekly doses of 500 mg. of chloroquine diphosphate will produce complete suppression of all forms of malaria and will provide a suppressive cure of malaria due to Plasmodium falciparum. Malaria due to P. vivax and possibly quartan infections, however, will produce clinical attacks several weeks after termination of suppressive therapy. For this reason, it is advisable to continue such therapy until return to an area in which adequate diagnostic and hospital facilities are available. It is well to avoid the consumption of raw salads, berries, and vegetables in areas in which sanitation is at a low level, including most parts of Africa. According to Jones (*Am. J. Trop. Med.* 1:576 [July] 1952), the danger of acquiring amebic infection from raw vegetables may be obviated to a considerable extent by soaking the vegetables in vinegar containing 5% acetic acid for at least 30 minutes at a temperature of 30 C (86 F). It is advisable also to boil all drinking water or to use one of the chlorine or iodine preparations for sterilization.

ENTERITIS IN TOURISTS

To the Editor:—*Many American tourists in Mexico have enteritis (usually mild) soon after arrival. As a rule, the general well-being and the appetite are not affected, but some patients have a great number of stools without tenesmus daily. What is the cause of this disease, and what is the best way of treating it?*

M.D., Wisconsin.

Answer.—Many factors may be involved in the enteritis occurring among tourists from the United States in Mexico. Ordinarily the cause is associated with staphylococcic or streptococcic contamination of food, with resulting production of chemical toxins which are highly irritating to the intestinal mucosa. The extent of the reaction seems to depend on the physical condition of the person involved, being more serious in fatigued persons. If the diarrhea continues, bacillary infection or amebiasis may be suspected. The diagnosis in these instances can be established only by repeated examination of stools. Salmonella infection may also occur.

Symptomatic treatment with bismuth magma and paregoric is usually satisfactory. Tea should be drunk frequently during recovery to restore fluid loss and reduce local irritation. If amebiasis occurs, specific therapy with carbarsone or iodochlorhydroxyquin is usually effective. In bacillary involvement, administration of an intestinal antiseptic, such as phthalylsulfathiazole or neomycin sulfate, is indicated.

Enteritis may be avoided by restriction of fluids to bottled beverages and by avoidance of fresh vegetables or fruits. Salad dressings, ice creams, pastries, and other foods that may become contaminated in handling should be avoided. Except at first-class hotels, tourists would be wise to eat only freshly prepared and well-cooked foods.

Answer.—The condition described is extremely common; it is sometimes called "tourist's disease" or "Aztec disease." Actually, there probably are several types of acute gastroenteritis that commonly afflict tourists and even natives in Mexico. Some of them are almost undoubtedly due to staphylococci or staphylococcus toxins; others are probably caused by Salmonella or other members of the paratyphoid group. It is important that the mild and temporary gostroenteritis not be confused with more serious infections which are also common in Mexico. Good results are often obtained with streptomycin therapy (1 Gm. in 20 cc. of salt solution, taken 10 or 15 drops at a time every hour); sulfadiazine and either paregoric or some other opium derivative with bismuth have been found effective. If the condition does not clear up in 48 hours with one of the appropriate treatments, it is wise to examine the patient for other conditions, particularly amebic dysentery or one of the paratyphoid diseases. The severity of the gastroenteritis varies widely, presumably because of differences in the number of germs or amount of toxin ingested and, possibly, in the degree of individual resistance.

ALCOHOLIC BEVERAGES AND ORALLY GIVEN HYPOGLYCEMIC DRUGS

To the Editor:—*A 58-year-old man has had an unusual reaction to chlorpropamide and tolbutamide. He has been a diabetic for 10 years and has been using NPH insulin, 30 units. He has a clinically determined myocardial insufficiency which warrants the use of anticoagulants and has been taking bishydroxycoumarin for one year. Recently he was placed on chlorpropamide therapy, 1½ tablets (375 mg.) daily, which brought his blood sugar level into the range of 128 mg. per 100 cc. About five days after initiation of this therapy he drank an alcoholic beverage, and within 10 minutes he felt a flush in the face, slight discomfort in the chest, and a desire to lie down. This passed in 45 minutes. Other persons in the room commented on the flush on his face and head. After being placed on tolbutamide therapy he had a similar, but milder, reaction after ingestion of alcohol. Can you comment on this reaction?*

M.D., Michigan.

Answer.—Flushing of the face and, at times, shortness of breath, palpitation, and nausea have been noted after ingestion of alcohol by patients receiving sulfonylurea compounds. Dolger reported that, among 500 patients who were treated with tolbutamide, there were 5 instances of marked face and body flushing after ingestion of alcoholic beverages (*Ann. New York Acad. Sc.* 71:275 [July 10] 1957). Such side-effects are relatively uncommon with use of tolbutamide but occur more frequently in patients receiving chlorpropamide. The *Annals of the New York Academy of Sciences* (vol. 74, March 30, 1959) includes reports on chlorpropamide, and several of these mention intolerance to alcohol as a side-effect. Blöch and Lenhardt (*ibid.*, pp. 954-961) reported intolerance to alcohol in 11.6% of 215 patients in whom the maintenance dosage of chlorpropamide was "usually 0.5 gm. or 0.25 gm., frequently given every other day." Of special interest is the article by Signorelli entitled "Tolerance for Alcohol in Patients on Chlorpropamide" (*ibid.*, pp. 900-903).

The exact mechanism of this untoward response is not understood. Prevention consists of abstinence from either alcohol or sulfonylurea compounds. In some patients the side-effects decrease even with continued use of the sulfonylurea agent, perhaps with decreased dosage.

WASHINGTON NEWS

New Administration Health Plan . .
Data on Health . .
Radiation Report . .

ADMINISTRATION OFFERS NEW HEALTH PROGRAM

Submission by the administration of its alternate health care program for the aged was expected to trigger congressional action on what has become a major political issue.

The Ways and Means Committee, which has the responsibility of originating legislation in the field, immediately started closed-door consideration of various plans to help the needy elderly meet medical-health bills. The Committee had postponed action until the administration came up with its own long-promised program.

The administration plan, presented by Arthur S. Flemming, Secretary of Health, Education, and Welfare, would cost the Federal government at least 600 million dollars annually. The states would pay about the same.

Under the option, the states and federal government would pay the benefits directly; under another, the state-federal contribution would offset part of the cost of purchasing private health insurance.

Except for those on the public assistance rolls, participants would have to pay part of the cost of health care themselves, including the first $250 of expenses.

The administration program was a rival plan to that of Rep. Aime Forand (D., R. I.), whose bill calls for providing health care financing for the elderly through the social security system. The controversial Forand bill, which has the backing of labor leaders, is strongly opposed by the administration, the medical and allied professions, and most business groups as unwieldy and constituting the entering wedge for complete government domination of medical practice.

The Ways and Means Committee, headed by Rep. Wilbur Mills (D., Ark.), had tentatively voted down the Forand proposal but were still considering compromise versions of it, as well as the administration program. It was expected to decide soon what course of action to take on the issue of health care for the aged.

Here are some details of the federal-state subsidy program offered by the administration:

ELIGIBILITY FOR PARTICIPATION

The program would be open to all persons aged 65 years and over who did not pay an income tax in the preceding year and to taxpayers aged 65 years and over whose adjusted gross income, plus social security, railroad retirement benefits, and veterans' pensions, in the preceding year did not exceed $2,500 ($3,800 for a couple).

ELIGIBILITY FOR BENEFITS

Persons eligible for participation would be entitled to the benefits if they paid an enrollment fee each year of $24 and after they had incurred health and medical expenses of $250 ($400 for a couple).

Public assistance recipients would be entitled to the benefits without paying the enrollment fee and with the states paying the initial $250 of expenses under the regular public assistance program.

BENEFITS

The Medicare program for the aged would pay 80% (100% for public assistance recipients) of the costs of the following comprehensive health and medical services for all participants who had established their eligibility, and where such services have been determined to be medically necessary: (1) hospital care—180 days; (2) skilled nursing home care—365 days; (3) organized home care services—365 days; (4) surgical procedures; (5) laboratory and x-ray services—up to $200; (6) physicians' services; (7) dental services; (8) prescribed drugs—up to $350; (9) private-duty nurses; and (10) physical restoration services.

OPTIONAL BENEFITS

Each state would provide that an aged person eligible for participation could elect to purchase from a private group a major medical expense insurance policy, with the understanding that 50% of the cost would be paid for him from federal-state matching funds, up to a maximum of $60. The state would be authorized to use appropriate private organizations as agents.

FINANCING

The governmental cost of the program would be financed by the federal government and the states on a matching basis. Federal matching would be 50%, on the average, with an equalization formula ranging from 33⅓ to 66⅔% for the federal share.

COST

Assuming that all states participate and that 80% of those who are eligible enroll for the program, it is estimated that the annual federal-state cost of this plan would be 1.2 billion dollars, with the federal share being estimated at 600 million dollars. There would be some reduction, to the extent that persons eligible for participation in the plan elected to purchase insurance policies providing for the optional benefits.

On the other hand, increases in costs and increased use of facilities over and above that included in the cost estimates could lead to an increase in these estimates. Also, there would be some

(Continued on next page)

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Lown, B., and Levine, S. A.:
Current Concepts in Digitalis Therapy, Boston,
Little, Brown & Company, 1954, p. 23, par. 2.

increase in federal payments for public assistance. This increase might reach 100 million dollars per year.

The make-ready cost during fiscal year 1960-1961—including grants to states to help them develop their programs—would be about 5 million dollars. The fiscal year 1961-1962 cost would depend on many factors. It was estimated that this would run in the neighborhood of 400 million dollars, of which 200 million dollars would be the federal share.

HEALTH STATISTICS REPORTED

The government has prepared a statistical digest on *Health, Education, and Welfare Trends* in order "to chart the gains of the past and to help in understanding current and emerging problems."

The digest, compiled by the Department of Health, Education, and Welfare, deals with a wide range of subjects. In it is noted that private expenditures for medical care and voluntary health insurance total about 5% of disposable personal income.

In 1958, per capita expenditures for medical care were nearly $96, distributed as follows: $30 for hospital services; $25 for physicians; $25 for medicaments and appliances, $10 for dentists, and $6 for all other medical expenditures.

Other facts cited were as follows:

Heart disease is the chronic condition people most often report for inability to carry on their usual occupation or major activity.

For each of the past two years hospital construction outlays reached almost 1 billion dollars. Four-fifths of the money was nonfederal.

In spite of reductions in recent years, there are still well over 600,000 resident patients of mental hospitals.

All federal grants-in-aid totaled 6.3 billion dollars in fiscal year 1959. Grants for health, education, vocational rehabilitation, welfare, and employment security accounted for 3.5 billion dollars of the total.

Copies of *Health, Education, and Welfare Trends* may be purchased from the Superintendent of Documents, U. S. Government Printing Office, Washington 25, D. C., at 50 cents per copy.

REPORT ON RADIATION HAZARDS

Government and private experts on radiation, summing up the latest scientific information on radiation hazards, reported that "as new information is gained, man can expect to derive increasing benefits from the release of nuclear energy with a minimum hazard to himself and his descendants."

A report issued by six committees of the National Academy of Sciences–National Research Council declared that "there are still many unknowns, and research on a wide front is needed." Some of the conclusions by the experts downrated public concern about possible dangers from radioactivity.

Some of the major findings were as follows:

There is some new evidence that genetic effects from low radiation doses might be less than previously estimated.

The committees continue to recommend that the average gonadal dose for the general population during the first 30 years of life not exceed 10 r (roentgens) of man-made radiation, and should be kept as far below this level as is feasible.

There is experimental evidence to show that radiation-induced tumors do not begin to develop immediately after the radiation has been absorbed.

No new evidence has appeared to show that nuclear tests have affected the weather.

The significant long-range effects of the presence of radioactive isotopes in foodstuffs remain to be determined.

The disposal of radioactive wastes has not resulted in any significant hazard to the public, its environment, or its natural resources.

There is nothing inherent in the radioactive-waste control problem to restrict the nuclear energy program, with adequate protection of public health and safety.

Present indications are that limited quantities of radioactive materials can be safely released in the oceans.

The reports resummarized the deliberations of committees on genetics, pathology, meteorology, agriculture and food supplies, disposal and dispersal of radioactive wastes, and oceanography and fisheries. They were appointed to conduct a continuing appraisal of the effects of atomic radiations on living organisms and to identify questions on which further intensive research was urgently needed.

MISCELLANY

The Agriculture Department offered to purchase 1,195,700 lb. of frozen, ready-to-cook poultry that had been treated with the chemical stilbestrol. The offer was made after the Food and Drug Administration banned the sale of such poultry in interstate commerce because stilbestrol can cause cancer in rats if fed in sufficient quantity. Only 1% of the nation's poultry crop was affected.

The Federal Trade Commission said the American Registry of Doctors' Nurses, Marianna, Fla., has agreed to stop using any trade name which falsely implies that it is a nonprofit organization without clearly and conspicuously revealing that it is a private business operated for a profit.

The House Veterans Affairs Committee approved a bill that would authorize for the first time the furnishing of outpatient care to veterans with non-service-connected disabilities. Under the legislation, this care could be provided when it is judged reasonably necessary in preparation for admission of the veteran who has been determined to need hospital care and who has been scheduled for admission and in cases in which a veteran with non-service-connected disabilities has been granted hospital care, and outpatient care is reasonably necessary to complete the treatment.

The Public Health Service announced a three-year study of hyptertension designed to test the effectiveness of various drugs in treating "essential hypertension," which accounts for most cases of high blood pressure. Five hospitals will share in research grants totaling $154,000 from the National Heart Institute.

An overdose of amphetamines taken by a truck driver was responsible for a truck-bus crash near Tucson, Ariz., last December, the Interstate Commerce Commission reported. Nine persons were killed in the accident. The government is carrying on a campaign against unauthorized sale of amphetamines.

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MEETINGS

AMERICAN MEDICAL ASSOCIATION: Dr. F. J. L. Blasingame, 535 North Dearborn St., Chicago 10, Executive Vice-President.
1960 Annual Meeting, Miami Beach, Fla., June 13-17.
1960 Clinical Meeting, Washington, D. C., Nov. 28-Dec. 1.
1961 Annual Meeting, New York City, June 26-30.
1961 Clinical Meeting, Denver, Nov. 27-30.
1962 Annual Meeting, Chicago, June 11-15.
1962 Clinical Meeting, Los Angeles, Nov. 26-29.

AMERICAN

1960

May

American Association for Cleft Palate Rehabilitation, Brown Palace Hotel, Denver, May 12-14. D. C. Spriestersbach, Ph.D., University Hospitals, Iowa City, Iowa, Secretary-Treasurer.

American Association on Mental Deficiency, Lord Baltimore Hotel, Baltimore, May 16-21. Mr. Neil A. Dayton, P. O. Box 51, Mansfield Depot, Conn., Executive Secretary-Treasurer.

American Association of Plastic Surgeons, Milwaukee Inn, Milwaukee, May 17-20. Dr. Thomas D. Cronin, 6615 Travis St., Houston 25, Texas, Secretary.

American Gynecological Society, W[illegible], Va., May 30-June 1. Dr. Andrew A. M[illegible], [illegible] Hosp., Washington 7, D. C., Secretary.

American Ophthalmological Society, The Broadmoor, Colorado Springs, Colo., May 16-18. Dr. Maynard C. Wheeler, 30 W. 59th St., New York 19, Secretary.

American Orthopaedic Association, The Homestead, Hot Springs, Va., May 30-June 2. Dr. Lee Ramsay Straub, 535 E. 70 St., New York 21, Secretary.

American Trudeau Society, Statler anl Biltmore Hotels, Los Angeles, May 16-18. Mr. Frank W. Webster, 1790 Broadway, New York 19, Executive Secretary.

American Urological Association, Inc., The Palmer House, Chicago, May 16-19. Mr. William P. Didusch, 1120 N. Charles St., Baltimore 1, Executive Secretary.

Hawaii Medical Association, Honolulu, May 12-15. Mr. Lee McCaslin, 510 S. Beretania St., Room 200, Honolulu 13, Hawaii.

Illinois State Medical Society, Hotel Sherman, Chicago, May 24-27. Dr. George F. Lull, 185 N. Wabash, Chicago, Secretary.

Massachusetts Medical Society, Statler-Hilton Hotel, Boston, May 17-19. Mr. Everett R. Spencer Jr., 22 The Fenway, Boston 15, Director of Public Relations and Administration.

Medical Library Association, Inc., Muehlebach Hotel, Kansas City, Mo., May 16-20. Miss Nettie A. Mehne, Upjohn Company Library, 301 Henrietta St., Kalamazoo, Mich., Secretary.

Minnesota State Medical Association, Kahler Hotel, Rochester, May 23-25. Mr. Harold W. Brunn, 496 Lowry Medical Arts Bldg., St. Paul 2, Executive Secretary.

National Tuberculosis Association, Statler & Biltmore Hotels, Los Angeles, May 15-20. Mr. James G. Stone, 1790 Broadway, New York 9, Executive Secretary.

Nevada Academy of General Practice, Reno, May 12-14. Dr. Roy M. Peters, 475 S. Arlington Ave., Reno, Nev., Program Chairman.

New Jersey, Medical Society of, Chalfonte-Haddon Hall, Atlantic City, May 14-18. Mr. Richard I. Nevin, P. O. Box 904, Trenton 5, N. J., Executive Officer.

Ogden Surgical Society, Ogden, Utah, May 18-20. Dr. O. E. Grua, 412 First Security Bank Bldg., Ogden, Utah, Secretary.

Ohio State Medical Association, Sheraton Cleveland, Cleveland, May 17-19. Mr. Charles S. Nelson, 79 E. State St., Columbus 15, Executive Secretary.

South Carolina Medical Association, Ocean Forest Hotel, Myrtle Beach, May 17-19. Mr. M. L. Meadors, 309 W. Evans St., Florence, S. C., Executive Secretary.

South Dakota State Medical Association, Alonzo Ward Hotel, Aberdeen, May 14-17. Mr. John C. Foster, 300 First Natl. Bank Bldg., Sioux Falls, S. D., Executive Secretary.

Symposium on the Psychological and Physiological Aspects of Space Flight, Southwest Research Institute, Hilton Hotel, San Antonio, Texas, May 26-27. For information write Mr. Jack Harmon, 8500 Culebra Rd., San Antonio 6, Tex., Public Relations Director.

June

American Academy of Tuberculosis Physicians, Miami Beach, Fla., June 11. Dr. George P. Bailey, P. O. Box 7011, Denver 6, Secretary.

American College of Angiology, Roney Plaza Hotel, Miami Beach, Fla., June 10-12. Alfred Halpern, Ph.D., 11 Hampton Court, Great Neck, N. Y., Executive Secretary.

American College of Chest Physicians, Miami Beach, Fla., June 8-12. Mr. Murray Kornfeld, 112 E. Chestnut St., Chicago 11, Executive Director.

American Diabetes Association, Inc., Hotel Deauville, Miami Beach, Fla., June 11-12. Mr. J. Richard Connelly, 1 E. 45th St., New York 17, Executive Director.

American Electroencephalographic Society, Belmont Hotel, Cape Cod, Mass., June 10-12. Dr. George A. Ulett, 1420 Grattan St., St. Louis 4, Secretary.

American Geriatrics Society, Americana Hotel, Miami Beach, Fla., June 9-10. Dr. Richard J. Kraemer, 2907 Post Road, Warwick, R. I., Secretary.

American Medical Women's Association, Hotel Carillon, Miami Beach, Fla., June 9-12. Mrs. Lillian T. Majally, 1790 Broadway, New York 19, Executive Secretary.

American Neurological Association, Hotel Statler, Boston, June 13-15. Dr. Melvin D. Yahr, 710 W. 168th St., New York 32, Secretary.

American Physical Therapy Association, Penn-Sheraton Hotel, Pittsburgh, June 26-July 2. Miss Lucy Blair, 1790 Broadway, New York 19, Acting Executive Director.

American Physicians Art Association, Miami, June. Dr. Kurt F. Falkson, 7 E. 78th St., New York 21, Secretary.

American Rheumatism Association, Hotel Diplomat, Hollywood-by-the-Sea, Fla., June. Mr. Gerard W. Speyer, 10 Columbus Circle, New York City, Executive Secretary.

American Society of X-Ray Technicians, Netherland Hilton Hotel, Cincinnati, June 11-16. Genevieve J. Eilert, R.T., 16 Fourteenth St., Fond du Lac, Wis., Executive Secretary.

American Therapeutic Society, Barcelona Hotel, Miami Beach, Fla., June 9-12. Dr. Oscar B. Hunter Jr., 915 19th St., N. W., Washington 6, D. C., Secretary.

Association for Research in Ophthalmology, Inc., Miami, Fla., June 12-17. Dr. Lorand V. Johnson, 10515 Carnegie Ave., Cleveland 6, Secretary-Treasurer.

Endocrine Society, Eden Roc Hotel, Miami Beach, Fla., June 9-11. Dr. Henry H. Turner, 1200 N. Walker, Oklahoma City, Okla., Executive Secretary.

Idaho State Medical Association, Sun Valley, June 15-18. Mr. Armand L. Bird, Sonna Bldg., Boise, Idaho, Executive Secretary.

Maine Medical Association, Hotel Samoset, Rockland, June 19-21. Dr. Daniel F. Hanley, P. O. Box 240, Brunswick, Maine, Executive Director.

Northwest Proctologic Society, Roche Harbor, San Juan Island, Wash., June 21-24. Dr. L. D. Leslie, 1162 Willamette St., Eugene, Ore., Secretary-Treasurer.

Society of Biological Psychiatry, Deauville Hotel, Miami Beach, Fla., June 11-12. Dr. George N. Thompson, 2010 Wilshire Blvd., Los Angeles 57, Executive Secretary.

Society for Investigative Dermatology, Inc., di Lido Hotel, Miami Beach, Fla., June 13-15. Dr. Herman Beerman, 255 S. 17th St., Philadelphia 3, Secretary-Treasurer.

Society of Nuclear Medicine, Estes Park, Colo., June 22-25. Dr. Thad P. Sears, Veterans Administration Hospital, Denver 20, Chairman.

Society for Vascular Surgery, di Lido Hotel, Miami Beach, Fla., June 12. Dr. George H. Yeager, 314 Medical Arts Bldg., Baltimore 1, Secretary.

July

American Goiter Association, Church House, London, England, July 5-8. Dr. John C. McClintock, 702 Madison Ave., Albany 8, N. Y., Secretary.

American Society of Facial Plastic Surgery, Hotel Elysee, New York City, July 22. Dr. Samuel M. Bloom, 123 E. 83d St., New York 28, Secretary.

Flying Physicians Association Hawaii Cruise, leaving Los Angeles and San Francisco, July 11. For information write Mr. Mark E. DeGroff, P. O. Box 3275, Tulsa, Okla.

Oregon Cancer Conference (Second Annual), Sheraton Hotel, Portland, July 7-8. Dr. Martin A. Howard, 115 S.W. Taylor St., Portland 5, Ore., Chairman.

Rocky Mountain Cancer Conference, Hilton Hotel, Denver, July 20-21. Mr. Harvey T. Sethman, 835 Republic Bldg., Denver 2, Executive Secretary, Colorado State Medical Society.

August

American Association of Blood Banks, Jack Tar Hotel, San Francisco, Aug. 21-26. For information write: AABB Central Office, Suite 1619, 30 N. Michigan, Chicago 2.

American Congress of Physical Medicine and Rehabilitation, Mayflower Hotel, Washington, D. C., Aug. 21-26. Mrs. Dorothea C. Augustin, 30 N. Michigan Ave., Chicago 2, Executive Secretary.

American Hospital Association, Civic Auditorium, San Francisco, Aug. 27-Sept. 1. Mr. Maurice J. Norby, 18 E. Division St., Chicago, Assistant Director.

American Institute of Ultrasonics in Medicine, Statler-Hilton Hotel, Washington, D. C., Aug. 20. Dr. Dorothy M. Stillwell, Dept. of Phys. Med. and Rehab., Univ. of Colorado Med. Center, Denver 20, Chairman.

American Physiological Society, Stanford University, Calif., Aug. 22-26. Mr. Ray G. Daggs, 9650 Wisconsin Ave., Washington 14, D.C., Executive Secretary.

American Society of Clinical Hypnosis, Miami, Fla., Aug. 7-10. Dr. Seymour Hershman, 6770 N. Lincoln Ave., Chicago 46, Secretary.

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FIFTEEN YEARS' EXPERIENCE WITH THE TUBERCULIN TEST

Samuel C. Stein, M.D.
and
Hubert W. Hetherington, M.D., Philadelphia

In order to restore confidence in the tuberculin test as such it is necessary to reinstitute the standardization of commercially available test materials. Satisfactory conditions of production, careful biological comparison, and electrophoretic analysis are necessary to insure the uniformity of the purified protein derivative (PPD) or of any tuberculin. From 25,538 records of patients examined during a 15-year period, data were obtained for a study of the relation of pulmonary tuberculosis to the results of tuberculin (PPD) tests. The data imply that the degree of sensitivity to tuberculin constitutes important information to the clinician. The authors conclude that the use of the standard two-dose test has been highly satisfactory and should not be modified in clinics that serve areas where tuberculosis continues to be a major public health problem.

ALTHOUGH there is agreement that the tuberculin test is important, there is disagreement regarding who should be tested, how often, by what method, by means of what material, in what quantity, and how the test results should be interpreted. Only too often, persons who have no special knowledge of the test express their opinions on these subjects; moreover, the test sometimes is given and its results are interpreted by persons who lack the necessary technical skill.

The earlier hope that tuberculin, either as a vaccine or as a desensitizing agent, would succeed in controlling clinical tuberculosis needs no discussion. In addition, subcutaneous injection of tuberculin is no longer used as a diagnostic procedure. A few physicians, in diminishing numbers, continue to regard tuberculin injections as specific therapy. As the frequency of infection and reinfection from persons who are sources of tuberculosis has decreased in recent years, however, the tuberculin test has become more valuable as a diagnostic procedure, while it continues to indicate the incidence of tuberculous infection in various groups of the population.

Methods of Tuberculin Testing

Unfortunately, there are numerous factors that interfere with a comparison of the results of the tuberculin tests which have been reported by different investigators in different decades. One of the chief of these is the use of various methods of testing. The first tuberculin test, introduced by Von Pirquet, was given by a so-called "scratch method,"

Assistant Professor of Medicine (Dr. Stein) and Associate Professor of Medicine (Dr. Hetherington), Henry Phipps Institute, University of Pennsylvania.

which permits unknown amounts of tuberculin to come in contact with the intradermal layers of the skin. A few years later Mantoux devised the intracutaneous test, which is generally considered to be the standard method of tuberculin testing. In addition, Vollmer's patch test, the Moro test which uses tuberculin-containing ointment, and the conjunctival test were applied by various investigators at different times. Recently, the Heaf test, given by a multiple-puncture method, is being used in a number of communities, chiefly in England.

A review of the various techniques used in administering tuberculin indicates that the Mantoux test has advantages that outweigh any alleged disadvantage. By this method, when properly applied, a uniform amount of standardized tuberculin can be given to each person being tested. Thus, variations of skin absorption or the possibility that an indeterminate amount of material may reach the intradermal layers of the skin can be resolved. Not only is the intracutaneous test most reliable, but its use permits a record of the intensity of the tuberculin reaction in different patients, and in the same patient at different times.

Synthetic-Medium Tuberculin

Among the factors that prevent results comparable to others with the intracutaneous test, the test material is important. For many years the material that was available was Koch's original tuberculin, namely, "Old Tuberculin" (OT). This material was used during a period when reports showed a high incidence of reactors in European cities and in large American cities.

It was a recognized handicap to standardization that OT, essentially the filtrate of a six-to-eight-week-old broth culture of tubercle bacilli, contained proteins and other substances from the broth medium. This handicap was eliminated by the production of synthetic mediums in which no protein was present. One of these mediums was originated by Long [1] while another, which produced a greater growth of bacilli, was devised by Dorset of the Bureau of Animal Industry.[2] The tuberculin from Dorset's medium was called synthetic-medium tuberculin. It was the ability to produce unadulterated tuberculoprotein that made possible further steps in tuberculin purification.

By putting synthetic-medium tuberculin through processes of ultrafiltration, filtration, precipitation by trichloracetic acid, centrifugation, removal of trichloracetic acid by extraction with ether, and dehydration, purified protein derivative (PPD) of tuberculin was first made. The final product is protein synthesized by the tubercle bacillus. Later, precipitation was accomplished with ammonium sulphate instead of trichloracetic acid. Precipitation with ammonium sulphate produces PPDS, the accepted standard of the World Health Organization and the commercial PPD that is available in the United States today. For clinical use the material is made into tablets containing known quantities of tuberculin.

Standardization

As late as 1923, the Bureau of Animal Industry, which had the function of testing the potency and stability of tuberculin in the United States, was using a relatively crude method of standardization which was described by White [3] as the guinea pig-killing method. About 1909, Roemer used Mantoux's intracutaneous method in cattle, the thickness of the skin determining the strength of the reaction. Lewis and Aronson [4] compared the reactions caused by the injection of a standard-strength tuberculin in one portion of the skin and the injection of a similar amount of the material to be tested (unknown tuberculin) in another portion of the skin of tuberculous animals. It is this method, modified for human subjects, that is now used to compare the potency of newly made tuberculin with a standard-strength tuberculin.

The original tests to compare OT and PPD were carried out chiefly between 1932 and 1936. By testing tuberculin reactors with OT given intracutaneously on one forearm and with PPD at a similar site on the other forearm, it was found that 0.1 cc. of diluent containing 0.01 mg. of the OT that had been used as a standard at the Phipps Institute for a number of years produced almost exactly the same reaction as the same amount of diluent containing 0.00002 mg. of PPD; an increase of 100 times, or 1.0 mg. of OT, was found to give the same reaction as an increase of 250 times the amount of PPD, namely, to 0.005 mg. of PPD.

To establish international standards, the World Health Organization has designated varying strengths of tuberculin in terms of units, namely: The equivalent of one international unit is 0.00002 mg. of PPD or 0.01 mg. of OT; the equivalent of 5 international units is 0.0001 mg. of PPD or 0.05 mg. of OT; the equivalent of 10 international units is 0.0002 mg. of PPD or 0.1 mg. of OT; and the equivalent of 100 international units is 0.005 mg. of PPD or 1.0 mg. of OT.

The use of intermediate test doses of PPD and of OT is already producing confusion. The term intermediate may apply to varying amounts, strengths, or units between 1 and 100. Some investigators are using 5 units and others 10 units as an intermediate test dose. Thus, results are obtained which do not lend themselves to comparison.

Even with a standard method and standardized tuberculin, different investigators, as well as the same investigator at different times or under different circumstances, have used varying amounts of test material. Originally the Mantoux skin test was given in three doses. The purpose was to avoid strong reactions in sensitive persons by starting with a small quantity of tuberculin. The first test dose was 0.01 mg. of OT; if this caused no reaction, a second test dose of 0.1 mg. of OT was given, and, in the absence of a reaction to this amount of tuberculin, a final injection of 1.0 mg. was given. If a person failed to react to 1.0 mg. of OT, he was considered tuberculin-negative. Later it was not uncommon for investigators to omit the second test dose and use two injections of 0.01 mg. and 1.0 mg. respectively. On the other hand, in communities where tuberculosis was less frequent, the first and third amounts (0.01 mg. and 1.0 mg. of OT) might be omitted, the investigator relying on a single injection of 0.1 mg. of OT to differentiate between tuberculin-positive and tuberculin-negative persons. These procedures may be regarded as use of an intermediate dose and use of variable doses, as mentioned above. One may question how many physicians have taken time to read the literature on this subject.

Originally the two-dose test was used to standardize purified protein derivative in the doses mentioned above. In view of the fact, however, that both 1.0 mg. of OT and 0.005 mg. of PPD are said to give nonspecific reactions because of their protein content and the cross reactions they cause in persons through sensitization by nonspecific protein, it is common practice to omit these test doses and to give either a single test dose of 0.1 mg. of OT or of 0.0001 mg. of PPD or to give a two-dose test with the intermediate amounts of tuberculin as the second and final dose. By avoiding the use of 1.0 mg. of OT and of 0.005 mg. of PPD, advocates of this method believe that they obtain specific reactions to tuberculin and that they do not fail to detect a significant percentage of persons with tuberculosis. There are others who feel that failure to use the larger doses of tuberculin in persons who fail to react to the smaller amounts merely avoids a difficulty, namely, having to make a clinical decision regarding the specific or nonspecific character of a reaction to the large dose.

In 1934 there were high hopes that PPD had solved the problem of a standard material for use in the intracutaneous test. At that time, there existed a committee of the National Tuberculosis Association that included members from commercial manufacturers of PPD. Long[5] states. "The conditions of manufacture are regulated by this committee. Neither the Purified Protein Derivative nor its process of manufacture is patented, although advantage is taken of an existing patent application in manufacture of the tablets. Under current arrangements the Committee endorses the use of a special designation, namely "Tuberculin, P.P.D. (Purified Protein Derivative)", by these two manufacturing houses, and the sponsorship of the National Tuberculosis Association is limited to their product. Continuous check on the character of the manufactured product is maintained by clinical trial of every lot manufactured, in the Henry Phipps Institute, under the supervision of Drs. Long, Seibert and Aronson."

These conditions existed up to 1951. Each new tuberculin supply was tested against standard PPDS, and the potency and stability of PPDS in tablet form was maintained. It was recognized that careful attention to each step in the production, as well as accurate evaluation of the resulting product, was necessary. Different strains of tubercle bacilli produce either different amounts of synthetic-medium tuberculin or tuberculins of different potency. In the absence of satisfactory conditions of production and a careful biological comparison, as well as of electrophoretic analysis, claims regarding the uniformity of PPDS or of any tuberculin may be open to serious question.

Tuberculin Test Technique

In addition to the lack of uniformity in the alleged dosage and potency of OT and PPD, a lack of meticulous care in the dilution of these products and their loss of strength due to deterioration of the materials in dilute solution may influence the results of the test. With the passage of time, both OT and PPD in dilute solution become weaker, although they may be kept for an indefinite period as concentrated OT or as PPD in tablet form. Nevertheless, the commercial producers put an expiration date on their packages. Methods of diluting OT and PPD have been described on numerous occasions. In giving injections of different strengths, the same syringe should always be used for a single strength of tuberculin, and it should not be used for any other purpose. Moreover, syringes should be cleaned with distilled water or buffer solution. Chemical particles that remain in syringes weaken dilute tuberculin that may be in contact with the glassware for several hours.

The technique of administering the intracutaneous test has remained unchanged throughout the years. The injection is given into the skin of the forearm. If the injection is too deep, or if the needle is not pushed into the skin in such a manner that the bevel is completely inserted and leakage of tuberculin results thereby, the reaction will be altered and the result misleading. A properly given injection causes an immediate, orange-peel-like, blanched wheal, which an experienced technician will recognize as the result of a properly given intracutaneous injection.

Although the interaction between the sensitized body cells of a tuberculous person and tuberculin is not a simple antigen-antibody response, reactions that occur to the first and to the intermediate doses of tuberculin are regarded as specific. Reactions to 1.0 mg. of OT or to 0.005 mg. of PPD may be nonspecific in some instances. A reaction to tuberculin is an allergic reaction, since it is acquired in response to a foreign protein within the body. The site of tuberculin injection is examined in 48 to 72 hours and the extent of edema (induration) is determined.

Determination of Intensity of Reaction.—A reaction accompanied by edema or induration measuring 10 mm. in diameter or less was considered a 1+ reaction; 11 to 20 mm. a 2+ reaction; and more than 20 mm. a 3+ reaction. Reactions accompanied by necrosis are designated 4+. If reactions to the first test dose, i. e., 5 mm. or less, were doubtful, the test was repeated with either the same test dose or the second test dose of PPD. Patients with doubtful reactions to 0.005 mg. of PPD were counted among the nonreactors. With severe reactions vesiculation may occur in the center of the edema, or actual necrosis may develop and heal, leaving a scar. Reactions accompanied by necrosis may be painful, while those associated with extensive edema without necrosis may cause marked pruritis.

Two highly trained technicians using Seibert-prepared PPD were solely responsible for making the tuberculin dilutions, the intracutaneous injections, and the subsequent interpretations of test results during the years of this study. For this reason, we believe that variations in results caused by subjective inconsistencies have remained constant and may be considered statistically insignificant.

Comment

During a 15-year period, from 1941 to 1955, 25,538 new patients were seen at the Henry Phipps Institute. By means of an IBM punch card system, 3,524 patients were subtracted from the total because they did not belong to the regular clinic population; they comprised patients of the special diagnostic and sarcoid clinics who lived outside the chest clinic area and a small group who, on the IBM cards, were wrongly punched as first-year clinic admissions, although they had been seen in a previous year. With deletion of these 3,524 from the total of 25,538, 22,014 patients remained. After exclusion of the above groups there is no reason to believe that significant variations in the criteria for admission to the clinic occurred during the years 1941 to 1955. The clinic roster was made up chiefly of tuberculous patients and their contacts, occasional patients with nonpulmonary tuberculosis, a small number with miscellaneous abnormalities, and patients with respiratory symptoms due to various causes. It is presumed that a part of the latter group had roentgenographic evidence of pulmonary abnormality that was diagnosed as pulmonary tuberculosis, despite failure to prove the specific etiology. In retrospect, it is our impression that this group may cause a slight variation in the figures given for the frequency of pulmonary tuberculosis and the tuberculin reaction correlation.

Cases of primary tuberculosis were ignored in our study, partly because of inconsistencies in this diagnosis in different years. A diagnosis of healed or calcified primary disease has no clinical significance, and a diagnosis of active primary tuberculosis, when made by roentgenographic examination alone, is often unconvincing. Cases of extrapulmonary tuberculosis in patients whose diagnosis and supervision usually originated from other institutions also were ignored. Fully aware that many factors are important in evaluating the tuberculin test, we intend to subject our statistical data to further analysis with regard to these factors.

Test results were not interpreted in 2,779 patients during the year of first admission to the clinic. In some instances patients were hospitalized immediately; in others they failed to return for interpretation of their test results in 48 or 72 hours. Among the latter were patients in whom the test had produced induration at indefinite periods after the 72-hour interval specified for interpretation. They were thus tuberculin-positive, but no accurate designation of the intensity of the reaction could be made. In other instances patients received the first test dose one or more times without a known reaction and without returning at a suitable interval for interpretation of the results. Moreover, there were times when vacation schedules or illness of the technician prevented administration of the tuberculin test.

Among the 2,779 patients whose tuberculin test results were unknown, 405, or 14.6%, had a diagnosis of pulmonary tuberculosis. The elimination of these 405 patients reduced the total of the diagnosed pulmonary tuberculosis cases from 3,620 to 3,215, a reduction of 12.6%.

Elimination of this group of 2,779 patients reduced to 19,235 the clinic population for whom interpretation of their reactions to the first test dose of 0.00002 mg. of PPD could be completed. There were 12,548 patients who reacted to this quantity of PPD, while 6,687 patients did not. Reactions to the second test dose of 0.005 mg. of PPD were interpreted in 5,756 patients, while in 931 instances the second test dose was either not given or no interpretation of results at 48 to 72 hours was obtained. Accordingly, it is not possible to add this group either to the reactors to the second test dose of PPD or to the group that failed to react to both test doses. They are designated by the term "1st test negative result, 2nd not interpreted" in tables 1, 2, and 3. The remaining 5,756 who did not react to the first test dose of PPD included 3,702 patients who reacted to the second, and 2,054 who reacted negatively to both tests. These figures are shown in table 1.

During the period from 1941 to 1955 there were major changes in the treatment of tuberculous patients and in the public health aspects of tuberculosis control. Treatment with antimicrobial drugs became increasingly prevalent during the latter half of the period, and there was a corresponding decrease in therapy by means of bed rest and artificial pneumothorax. It is generally believed that conversion of sputum by chemotherapy has greatly reduced the number of tuberculous patients who expel virulent tubercle bacilli; this, in turn, has resulted in a decrease in the opportunities for tuberculous infection, and hence in a much more rapid decline in the number of tuberculin reactors than would have been the case with the relatively slower decline that was occurring prior to use of antimicrobial methods of tuberculosis control.

Table 1.—*Results of Tuberculin (PPD) Tests in Patients at Henry Phipps Institute, Philadelphia, 1941-55*[*]

		Reactors to PPD				Nonreactors to PPD			
		1st Dose, 0.00002 Mg.		2nd Dose, 0.005 Mg.		1st Test Result Negative, 2nd N.I.†		Both Test Results Negative	
Yr.	Total Tested	No.	%	No.	%	No.	%	No.	%
1941-55	19,235	12,548	65.2	3,702	19.2	931	4.8	2,054	10.7
1941-45	6,247	4,211	67.4	1,275	20.4	170	2.7	591	9.4
1946-50	7,579	4,749	62.6	1,527	20.1	510	6.7	793	10.5
1951-55	5,409	3,588	66.3	900	16.6	251	4.6	670	12.4

[*] Excluding 2,779 patients not given a tuberculin test during year of 1st admission.
† N.I.: not interpreted.

The considerable effect of antimicrobial therapy is clearly seen in the mortality[6] and is less noticeable in the morbidity.[7] The results of a joint effort in tuberculin testing by the Philadelphia Tuberculosis and Health Association, the Philadelphia Board of Education, and the Philadelphia Department of Public Health were reported at a recent symposium.[8] During the 1958-1959 school year, about 11,000 first-grade pupils were given intracutaneous tests with 0.00002 mg. of PPD, and 1.9% had reactions with induration of 5 mm. or more in diameter. In 1928 a tuberculosis case-finding study in Philadelphia school children revealed a tuberculin reactor rate at the age of 7 years of 24.6% to test doses of 0.01 mg. of OT.[9] Since table 1 fails to show a decrease in the infection rate in the three five-year periods, the continued high incidence of reactors is probably a result of well-directed efforts in tuberculosis case finding in an area of high epidemiologic significance.

Table 2.—*Pulmonary Tuberculosis in Tuberculin-Tested Population*[*]

Year	No. of Reactors to 1st PPD Dose, 0.00002 Mg.	Diagnosis Pulmonary Tuberculosis		No. of Reactors to 2nd PPD Dose, 0.005 Mg.	Diagnosis Pulmonary Tuberculosis		1st Test Result Negative 2nd N.I.,†	Diagnosis Pulmonary Tuberculosis		Both Test Results Negative,	Diagnosis Pulmonary Tuberculosis	
		No.	%		No.	%	No.	No.	%	No.	No.	%
1941-55........	12,548	3,005	23.9	3,702	139	3.7	931	31	3.3	2,054	40	1.9
1941-45........	4,211	929	22.1	1,275	34	2.7	170	9	5.3	591	11	1.9
1946-50........	4,749	1,013	21.3	1,527	54	3.5	510	10	2.0	793	20	2.5
1951-55........	3,588	1,063	29.6	900	51	5.7	251	12	4.8	670	9	1.3

[*] In 2,779 patients not tested, pulmonary tuberculosis was diagnosed in 405.
† N.I.: not interpreted.

Further analyses of the data are shown in table 2. An attempt was made to determine the incidence of pulmonary tuberculosis in the tuberculin-tested population. It is evident that only a small percentage of tuberculous patients fails to react to the first test dose and that an even smaller percentage fails to react to both test doses. The statistics are purposefully depicted in their most unfavorable aspect, since we have taken a percentage of tuberculin test "failures" in relation to the clinically diagnosed population. If we were to compare the patients with pulmonary tuberculosis who failed to react to the first test dose of PPD with the total tested population, the percentage of failure would be greatly reduced. Thus, in this highly selected population drawn from the chest clinic, the number of tuberculosis patients who failed to react to the first test dose of PPD was 210, or 1.1%, of 19,235 tested persons. Of these 210 patients, 139 reacted to the second test dose, leaving only 71, or 0.4%, who failed to react or who belonged in the category "1st test negative result, 2nd not interpreted." Table 3 shows that 6.5% of patients with a clinical diagnosis of pulmonary tuberculosis failed to react to the 0.00002-mg. dose of PPD. One per cent of tuberculous patients (table 3) did not receive the second test dose. Had the second test dose of PPD been given, it is obvious that a number of patients would be added to those who reacted to the second test dose, and an addition also would be made to the number who reacted negatively to the second test dose. Since the percentages of nonreactors to the first test dose shown in table 3 are of the order of 7 to 2, it may be inferred that seven-ninths of the 31 patients would have reacted to the second test dose and that the remaining two-ninths would have failed to react; thus, the percentage of tuberculous patients reacting to the second test dose may be assumed to be 5.1, while those reacting negatively to the second test dose will constitute 1.4%.

Table 3.—*Results of Tuberculin (PPD) Tests in 3,215 Patients with Pulmonary Tuberculosis*

Reaction to Test Dose of PPD	No.	%
Positive to 1st, 0.00002 mg.	3,005	93.5
Positive to 2nd, 0.005 mg.	139	4.3
Negative to 1st, 2nd not interpreted	31	1.0
Negative to both	40	1.2

It has been implied that the degree of sensitivity to tuberculin may be of clinical significance. Table 4 constitutes an attempt to determine if this impression can be affirmed or denied. It is readily seen that most tuberculous patients who react at all have strongly positive reactions. Almost two-thirds of them had 3+ reactions, and an additional 25% had 2+ reactions to the first test dose of PPD. On the other hand, 8% exhibited less than a 2+ reaction to the first test dose (0.00002 mg.) of PPD.

In table 4, the high incidence of reactors to PPD in the nontuberculous group is compatible with the expected prevalence of infection in a district with high morbidity and mortality. The fact that most nontuberculous patients have 2+ or 3+ reactions to the first test dose may be attributed to the large number of contacts in the clinic population.

The data imply that the degree of sensitivity to tuberculin constitutes important information to the clinician. In the selected population pulmonary tuberculosis was found to occur in slightly less than 25% of patients who, given 0.00002 mg. of PPD, had reactions of 2+ or more, while tuberculosis was found in 15.8% of 1+ reactors to 0.00002 mg. of PPD, in 6.6% of 3+ reactors to 0.005 mg. of PPD, and in 1.9% of 2+, 1+, and nonreactors to 0.005 mg. of PPD.

Aronson[10] has pointed out that "the sensitivity to tuberculin induced by the intracutaneous administration of BCG vaccine is not as marked as that resulting from natural infection. This is indicated by the smaller per cent of the vaccinated who reacted to the initial dose of 0.00002 mg. of PPD and the less severe local reaction in the vaccinated than was noted in the controls who reacted."

Noninfected persons who were vaccinated with BCG in the clinic usually showed, in six to eight weeks, a 2+ or a 1+ reaction to 0.1 mg. of OT, or a reaction to the second test dose of PPD. These reactions tended to remain constant for months or years.

TABLE 4.—*Degree of Sensitivity to Tuberculin (PPD) in Tuberculous and Nontuberculous Patients**

Diagnosis	No. of Reactions to Test Doses of PPD by Intensity								
	1st, 0.00002 Mg.				2nd, 0.005 Mg.				
	4+	3+	2+	1+	4+	3+	2+	1+	Total
Tuberculosis	7	1,926	926	146	2	93	32	12	3,144
Nontuberculosis ..	23	5,952	2,789	779	5	1,313	1,649	596	13,106
Total	30	7,878	3,715	925	7	1,406	1,681	608	16,250

* An additional 71 patients with pulmonary tuberculosis failed to react to both test doses of tuberculin or failed to react to the first test dose and did not return for the second test reading; there were 2,914 nontuberculous patients in these categories.

The occurrence of natural superinfection was shown by an increase in the intensity of the reactions to 2+ or more to 0.00002 mg. of PPD. The constant and uniform results that Aronson obtained were, in all probability, due to the routine method used in subculturing the original strain of BCG he had acquired, as well as in the routine bioassay of the vaccine.

Table 5 presents data on 3,144 patients with pulmonary tuberculosis, which in 1,018 (32.4%) is of minimal degree, in 1,207 (38.4%) moderately advanced, and in 919 (29.2%) far advanced.

It has been pointed out that 8% of patients with pulmonary tuberculosis either had 1+ reactions to the first test dose of PPD or failed to react to this amount of test material. It follows that most tuberculous patients have strong reactions. Thus, in table 5, there were 88% of patients in the minimal group who had 2+, 3+, or 4+ reactions to the first test dose, while 91.8% in the moderately advanced group, and 92.3% in the far-advanced group, had reactions indicating similarly high tuberculin sensitivity.

TABLE 5.—*Relation Between Degree of Sensitivity to Tuberculin (PPD) and Extent of Pulmonary Tuberculosis, 1941-55*

Diagnosis Extent of Pulmonary Tuberculosis	No. of Reactions to Test Doses of PPD by Intensity								
	1st, 0.00002 Mg.				2nd, 0.005 Mg.				
	4+	3+	2+	1+	4+	3+	2+	1+	Total
Minimal	1	645	251	61	0	42	11	7	1,018
Moderately advanced	5	785	323	46	1	34	12	1	1,207
Far-advanced	1	496	352	39	1	17	9	4	919
Total	7	1,926	926	146	2	92	32	12	3,144
%	0.2	61.3	29.5	4.6	0.1	2.9	1.0	0.4	100

This analysis indicates that the extent of pulmonary disease is not the factor that determines the intensity of reaction. We infer that, in all probability, *the local reaction to the tuberculin test is* a manifestation of systemic invasion by tubercle bacilli; hence, the extent of focal pulmonary tuberculosis does not materially, of itself, influence the intensity of the reaction.

Summary and Conclusions

The tuberculin test is a means of indicating proper direction in case-finding and in local tuberculosis control programs. The use of the standard two-dose test has been highly satisfactory and should not be modified in clinics that serve areas where tuberculosis continues to be a major public health problem. The data imply that the degree of sensitivity to tuberculin constitutes important information for the clinician.

We are of the opinion that loss of confidence in the tuberculin test has occurred. The techniques of administration and interpretation are local problems, but restoration of confidence in the test as such requires reinstitution of standardization of commercially available test materials. Today, as in the past, the tuberculin test is a cornerstone in the control of tuberculosis.

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HEATED HYPERTONIC AEROSOL IN COLLECTING SPUTUM SPECIMENS FOR CYTOLOGICAL DIAGNOSIS

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The cytological examination of sputum is a valuable diagnostic aid, but the necessary specimens have not always been readily obtainable. A new technique involving the inhalation of an aerosol was devised, the inhalant consisting of 10% sodium chloride in 15% propylene glycol. It was used in 20 patients and yielded between 1 and 10 cc. of sputum in every one of 45 trials. Thirty-three of the 45 specimens were satisfactory for cytological examination. None of these patients had given satisfactory specimens before. This procedure is suggested for use especially in patients with suspected malignant pulmonary disease.

It has been known since 1918, when Hampeln[1] first described the presence of malignant cells in the sputum of patients with bronchogenic carcinoma, that cytological examination of sputum could be used as a diagnostic tool. The routine examination of sputum for abnormal cells was greatly advanced by the technique of Papanicolaou,[2] described in 1943. Since that time many reports have appeared in the literature concerning this technique.

The over-all accuracy of the method and the number of specimens necessary to obtain maximum diagnostic accuracy has varied with the laboratory reporting. Liebow, Lindskog, and Bloomer[3] noted an accuracy of 42.8% in proved cases of bronchogenic carcinoma when an average of 3.2 specimens per patient were examined. McDonald and Woolner[4] stated that three specimens per patient should be examined. They estimated their accuracy at 50% on sputum samples, with a 10% increase in accuracy if bronchial washings were also examined. Farber and his group[5] reported an over-all accuracy of 55% in 241 cases of proved bronchogenic carcinoma, with the accuracy increased to 90% if five or more specimens were examined. Papanicolaou's[6] cases revealed an over-all accuracy of 94.5% in 54 patients studied. In this group there were three false-negative and no false-positive results.

In spite of this variance in reported diagnostic accuracy, there is general agreement that the cytological examination of sputum is a worthwhile diagnostic measure. It serves as an adjunctive procedure to be used along with direct bronchoscopic

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washing and biopsy in patients suspected of having lung cancer. It increases the number of positive diagnoses which can be established and permits earlier diagnosis in many instances. There is general agreement that the cytological examination of three or more sputum specimens greatly decreases the number of false-negative diagnoses.

When patients with suspected malignancy are raising sputum, the collection of specimens for cytological examination is usually no problem. Adequate preparations for microscopic study can be made easily if the specimens are promptly brought to the laboratory in their fresh state and are handled in the generally prescribed manner.[7] The fact that sputum originates from the lower respiratory tract can then be confirmed by the demonstration in the cytological smears of histiocytes or alveolar phagocytes, which usually contain carbon pigment (fig. 1). When these cells are absent, one cannot be certain that the secretions are not all from the trachea or upper respiratory passages, and such specimens are reported as unsatisfactory for diagnosis of bronchogenic carcinoma. This study is concerned with patients who do not raise sputum or whose sputum specimens have been reported as unsatisfactory for diagnosis because of a lack of histiocytes in the cytological smears.

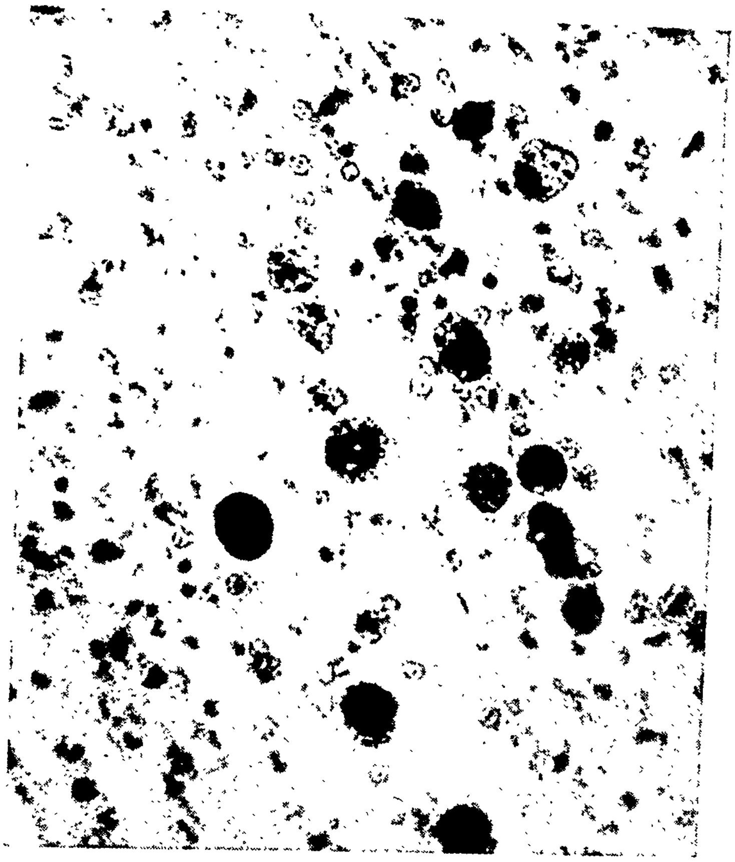

Fig. 1.—Histiocytes containing dark (carbon) particles. These cells must be present to indicate that specimen originated in lower respiratory tract.

At our hospital it has been the custom to perform peroral bronchial washings on those patients with suspected pulmonary malignancy who were not raising sputum or who had produced unsatisfacto specimens. This procedure is performed without a drugs or anesthesia. The patient is placed in sitti position with the mouth widely opened and t tongue extended. He is instructed to breathe in a out rapidly; as the glottis opens, isotonic sodiu chloride solution is instilled into the trachea. Th stimulates the patient to propellent cough, and t expelled secretions are collected. These peror bronchial washing specimens have been difficult work with because of their watery character, an the yield of satisfactory specimens has been low. the past we have administered various aerosol sol tions at room temperature in an attempt to produ sputum for cytological examination. Bronchodilat drugs, isotonic sodium chloride solution, and we ting agents have been used with some success, b the percentage of patients from whom satisfactor specimens could be obtained has been low.

In 1958 Bickerman, Sproul, and Barach [8] reporte the use of a heated hypertonic saline aerosol to col lect sputum specimens for cytological examinatio They used a solution which contained between 3 and 15% sodium chloride to which 15% to 20 propylene glycol was added, and they administere it with an electrically heated high capacity aeroso unit. Using this technique they were able to obtai sputum from 82.5% of a consecutive series of 33 patients who were either normal, had chronic pul monary disease, or were suspected of having pul monary malignancy. They subjected 74 of thes specimens to cytological examination, and 78.4 were found to be satisfactory by the criteria alread outlined. They did not indicate how many of thei patients were spontaneously raising sputum.

The present study was initiated in an attempt to evaluate the heated, hypertonic aerosol method of obtaining sputum for cytological examination with the aim of improving our present yield of satisfactory specimens.

Methods and Materials

A heated nebulizer which delivers a liquid and vapor mist at a temperature of 105 F (40.6 C) was used. A solution of 10% sodium chloride in 15% propylene glycol was nebulized either with oxygen at a flow rate of 5 to 7 liters per minute or with an electric diaphragm air compressor as the propellant.

A Y-shaped glass tube was inserted in the tubing system connecting the nebulizer to the air source (fig. 2). With the mouth closed over the nebulizer mouthpiece and the index finger placed over the open end of the Y-shaped tube, the patient was instructed to inhale rapidly and deeply. The mouth was then removed from the mouthpiece and the finger taken off the tube during normal expiration. This procedure was repeated with each breath for a period of 10 to 15 minutes; the patient rested for a few moments if there were any symptoms due to hyperventilation. With use of this technique, 4 to 7 cc. of aerosolized material was delivered per treatment period.

All sputum raised from the time of initiation of the aerosol until one hour after its termination was collected. If there was no spontaneous cough, the patient was instructed to cough voluntarily in an effort to raise sputum. Specimens so obtained were promptly sent to the laboratory where they were handled in the usual manner.[7]

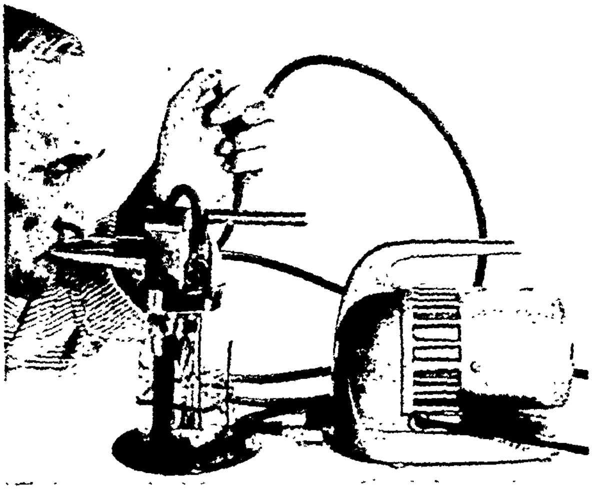

Fig. 2.—Heated nebulizer with Y-shaped tube adaptor connected to portable air compressor.

Patients selected for study were those suspected of having pulmonary cancer, who were not raising sputum or had previously, on more than one occasion, produced specimens which were unsatisfactory for cytological examination. Patients who were producing multiple satisfactory specimens were excluded from the study.

In evaluating this technique, we compared our results with the results of examination of various types of specimens obtained by the cytology division of the pathology department.

Results

A series of 20 patients was studied, and 45 aerosolizations were performed. The mean age was 63 years, and 16 of the patients were over the age of 50 years. Sputum was produced on every occasion in amounts varying between 1 and 10 cc. Thirty-three (73.3%) of the 45 specimens were satisfactory for cytological examination by the criteria previously outlined (see table). In this group of 20 patients, showed positive findings in one patient, suspicious findings in two, and negative findings in the fourth. On no occasion did we obtain as many as five specimens from any one patient. This series is too small to permit evaluation of the accuracy of cancer diagnosis by cytological examination.

The specimens were similar to naturally produced sputum in ease of handling, and no cellular distortions were noted. No side-effects were encountered in any of our patients. Most of the patients could carry out the procedure without assistance or supervision after the initial instructions. As experience with the technique was gained, it became apparent that satisfactory specimens could be obtained from almost any patient who could adequately inhale the aerosol.

A review of the record of the cytology division of the pathology department for the period of July through December, 1958, revealed that 338 specimens, including sputum, peroral bronchial washings, and bronchoscopic smears, were examined. These were unselected cases, with no distinction being made between sputum producers and nonproducers. In this group 213 (63%) of the specimens were satisfactory.

In the group of patients studied on the chest service of the hospital during the 18-month period from Jan. 1, 1958, through June 30, 1959, there were 22 patients who underwent peroral bronchial lavage to obtain specimens for cytological examination. A total of 58 washings were performed, and only 25 (43.1%) of the specimens were satisfactory.

Comment

Nebulization of cold (room temperature) isotonic fluids produces aerosols which are at 30 to 60% of body humidity (absolute humidity [water content] of saturated air at body temperature, 98.6 F [37 C]), with roughly one-half of the water in vapor form and one-half as suspended water droplets. By raising the temperature of the aerosol as it leaves the generator to 100 to 105 F (37.8 to 40.6 C) and by increasing the tonicity of the solution with sodium chloride and propylene glycol, it is possible to get aerosols which are at or above body humidity. Raising the temperature of the aerosol increases the amount of water vapor which the air will hold.[9]

Comparative Incidence Specimens Satisfactory for Cytologic Examination

Study	Technique	Patients, No.	No.	Specimens No.	%
Present study	Heated aerosol	20	45	33	73.3
Bickerman et al[7]	Heated aerosol	74	74	58	78.4
Michael Reese Hospital, Cytology Service (July-Dec., 1958)	Various	...	338	213	63
Michael Reese Hospital, Chest Service (Jan., 1958-June, 1959)	Peroral bronchial washings	22	58	25	43.1

The higher tonicity of the solution results in lowering vapor pressure so that the tendency for tiny fluid droplets (0.5 to 1.0 μ with this machine) to rapidly turn into vapor is markedly decreased. A stable suspension of fluid droplets in saturated air is thus produced. Many of these droplets are then carried to the lower air passages, where they are deposited. In the bronchi and bronchioles the hypertonic solution will have a mild irritant effect which increases mucus secretion. There may also be some osmotic transudation of fluid through the bronchial mucosa. This increased quantity of bronchial fluid provides a vehicle for the expectoration of exfoliated cells.

A warm solution does not have the irritant effect of a cold, hypertonic solution on the posterior pharynx and is able to reach the lower respiratory passages without producing discomfort or undesirable side-effects higher in the respiratory tree. At the lower levels, the mildly irritating effect of the hypertonic aerosol will stimulate cough in many patients.

Our results with this aerosol method were essentially the same as those of Bickerman, Sproul, and Barach.[8] Our yield of 73% satisfactory specimens was slightly better than the 63% yield in the total experience of our cytology service. However, this 10% increase in the number of satisfactory specimens with use of the aerosol technique assumes greater importance when one considers that our series included only patients who were not producing sputum or who had previously produced unsatisfactory specimens by the usual techniques.

In comparison with the results obtained by peroral bronchial washing, results of the aerosol method were clearly superior. It is a comfortable technique which can be easily administered by a technician. There are no significant side-effects, and there is no hazard of explosive cough. It can be used without fear on older, debilitated persons. This simple, safe technique should replace the more cumbersome approach of peroral bronchial lavage in patients who are not raising sputum.

The extension of this method to collection of sputum specimens for bacteriological diagnoses by altering the solution is now under consideration.

Summary

A heated hypertonic aerosol solution of 10% sodium chloride in 15% propylene glycol was used to collect sputum specimens for cytological examination from a group of patients with suspected pulmonary malignancy who were not raising sputum or who had previously produced unsatisfactory specimens. Twenty patients received the heated aerosol a total of 45 times; sputum was produced in all attempts. Thirty-three of the 45 specimens (73.3%) were satisfactory for cytological examination. The technique is a simple, safe approach to the problem of sputum collection in these patients and can be used as a routine procedure. It is far superior to peroral bronchial lavage and should supplant that method of obtaining specimens for cytological examination.

Addendum

Since the original manuscript was submitted for publication this technique has been established as a routine procedure. The aerosol is administered by technicians of the oxygen inhalation service. Since the initiation of this service 112 patients of all types (sputum producers and nonproducers) have received the hypertonic aerosol a total of 290 times; 251 of the specimens (86.5%) have been satisfactory for cytological examination. In this group of patients six have been found to have malignant cells in their sputum by use of the aerosol technique.

29th St. and Ellis Ave. (16) (Dr. Snider).

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RATIONAL TREATMENT OF ANEMIAS.—When anemia is suspected we should first of all determine whether or not the patient really has anemia and in so doing we must exercise care to employ reliable methods. If the patient is anemic, we should do everything possible to determine the cause. Once the cause is found the anemia should be treated as specifically as possible, usually with a single substance such as vitamin B_{12}, ferrous sulfate, corticosteroids and in some instances by operative procedures such as splenectomy. Shotgun hematinic preparations should be avoided like the plague.—L. E. Young, M.D., Pitfalls in the Management of Chronic Anemia, *Medical Record and Annals*, March, 1960.

ROENTGENOGRAPHIC FINDINGS IN AN EARLY CASE OF LINITIS PLASTICA

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The typical roentgenographic aspect of linitis plastica has been that of "leather bottle stomach." This study describes roentgenographic signs that appear before this deformity. The clinical history of a 44-year-old woman included complaints of heartburn and mild gastric pains but no other signs of serious disease. Roentgenographic examination showed a hook-formed stomach, with abnormalities limited to an irregular area on the greater curvature. Here the mucosa had an irregular surface, whereas normal folds were found everywhere else. Peristalses passed over the lesion, and the rest of the greater curvature was pliable. At operation, an early stage of linitis plastica was found.

Linitis plastica was first described by Lewis Briston in 1854 as a diffuse, rarely circumscribed increase in the connective tissue of the stomach, causing a marked thickening of the wall of the stomach. Clinically the disease is characterized by an insidious onset, a slowly progressing cachexia, and a fatal termination.[1] Although this condition is not rare, very few reported cases have been diagnosed at an early stage.

Report of a Case

History.—A 44-year-old woman was first seen by us in June, 1958. She appeared to be in good general physical condition and looked about 15 years younger than her age. For the previous three years she had had pains in the epigastrium when hungry. These pains were relieved by food. She complained of frequent nausea and constipation. There was neither weakness nor loss of weight. Four months prior to our examination, she had complained of midback pain which was diagnosed elsewhere as "arthritis of the spine." For this she was hospitalized at an orthopedic hospital for two weeks. A moderate loss of appetite and a pain in the epigastrium radiating to the back persisted.

Symptoms.—When seen by us in June, her complaints were spasms in the epigastrium radiating to the back and constant "sour stomach," with a desire to belch but without the ability to do so. There was no abdominal distention. During the past year she had had two gastrointestinal roentgenographic examinations at two different hospitals. The last one was performed six months prior to our consultation. These examinations were reported as revealing no pathology.

Physical examination revealed a definite tenderness in the epigastrium. No abdominal mass was present. The liver and spleen were not enlarged. No nodes were palpably enlarged.

The roentgenographic examination by one of us (F. J. L.) revealed a normal esophagus. The stomach filled without delay in hook form and was of normal size and position (fig. 1). The lesser curvature seemed to be normal. In the middle of the greater curvature, there was an area of about 7 cm., with irregular outline, serrated, and with some pliability. There was some elasticity of the stomach wall, but the stomach did not distend entirely normally in this region. At one point (fig. 2), a niche-like protrusion was visible on spot films. The study of the gastric mucosa (fig. 3) revealed normal folds in the upper portion of the stomach, terminating abruptly. In the region of the previously reported defect, the mucosa was irregular and cobblestone-like in appearance. The antrum, from the angulus on (distally), was normal on complete filling and on mucosal studies. The duodenal bulb was normal. These findings were suggestive of an infiltrative lesion of the middle portion of the stomach, especially along the greater curvature, probably a carcinoma. Since the gastric wall was not completely rigid, the findings were difficult to evaluate. The gastric mucosa and greater curvature showed deformity without complete rigidity (compare fig. 1, 2, and 3). It was felt that surgery was indicated.

Several months after the operation, films which had been taken in December, 1957, in one of the hospitals were made available to us. These films, as mentioned above, had been reported as showing no abnormalities. On reviewing the roentgenograms, however, changes of the mucosa of the stomach can be seen (fig. 4). The upper part of the stomach shows normal mucosa. In the middle portion, nodular changes are present. On complete filling of the stomach (fig. 5), a small defect on the greater curvature of the stomach is visible. Comparing the two sets of examinations, the progress of the disease is visible.

Operative Findings.—An operation was performed by one of us (H. J. H.) on July 9, 1958. The abdomen was entered through a transverse, inverted "V" incision. Exploration of the abdomen was carried out, with essentially negative findings other than those in the stomach. The major portion of the antrum and the body of the stomach were densely infiltrated with a firm tumor. This extended to, but not into, the fundus. The lesion appeared to ach to within 4 cm. of the pylorus and did not xtend beyond it. There were several enlarged ymph nodes on the lesser curvature of the stomach which were removed with the specimen. No other enlarged lymph nodes were encountered. The liver was free of disease.

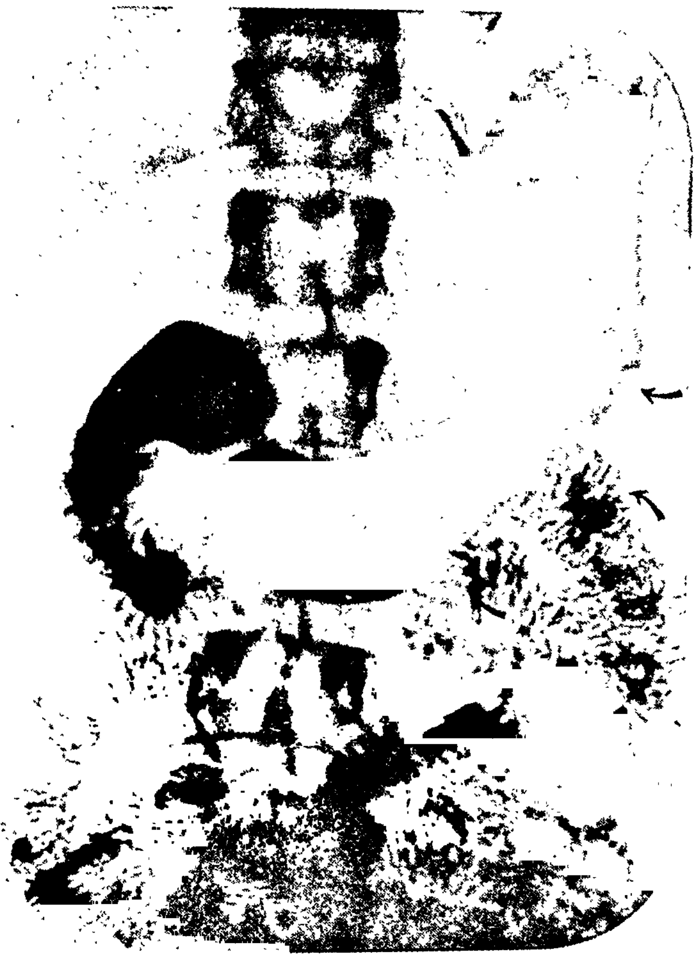

Fig. 1.—Complete filling of stomach: note shallow irregularity in middle of greater curvature.

A gastrectomy was performed in which, together with the stomach, the omentum, the gastrocolic omentum, and the lesser omentum with the lymph nodes contained therein were removed. Since the line of resection was found to be 1 cm. from the tumor, a more extensive resection was carried out, with removal of an additional 3 to 4 cm. of stomach and leaving only a small rim of stomach attached to the esophagus. About 1 in. of duodenum was excised, and the distal duodenum was then closed by inversion. A loop of jejunum, about 8 to 10 in. from the ligament of Treitz, was brought up anterior to the colon and anastomosed end to side to the small rim of stomach that remained attached to the esophagus. To perform the anastomosis it was necessary to extend the incision vertically upward in the midline. The tumor was determined to be linitis plastica by frozen section at the time of operation.

Postoperative Course.—The patient had a relatively benign postoperative course. Her condition gradually improved, and she was able to eat increasingly well as time went by. By the time of discharge on July 30, 1958, she was eating a regular diet in six daily feedings.

Pathologist's Report.—Details of the pathological report were as follows:

Gross Pathology: The specimen consists of a segment of stomach measuring, after resection, 19 cm. in length along the greater and 12 cm. along the lesser curvature. Attached is the pyloric ring and about 1.5 cm. of normal duodenum. Separate is a 3-cm. rim of stomach, which is mainly from the lesser curvature. There is no evidence of neoplasm within this strip. Within the stomach, involving the greater curvature, anterior and posterior walls, and extending up to the lesser curvature there is notable thickening of the gastric wall, up to about 13 mm. in greatest thickness. Along the greater curvature are two superficial ulcerations within the thickened areas of stomach. The lesion appears to extend grossly to within 4 cm. of the pyloric ring and proximally to within 1 cm. of the proximal line of resection. A 22-cm. segment of normal greater omentum is present. Nine lymph nodes up to 15 mm. in greatest diameter are present, all of which are sectioned for histological study.

Histology: Sections reveal the presence of a diffuse neoplasm involving the gastric wall. The neoplasm invades from the mucosa through the submucosa and the muscularis into the adjacent fat. The neoplasm is composed of polyhedral-shaped epithelial cells exhibiting hyperchromatism and macrocytosis. There is a tremendous desmoplasia involving the submucosa as well as the muscularis. It is difficult to encounter neoplastic

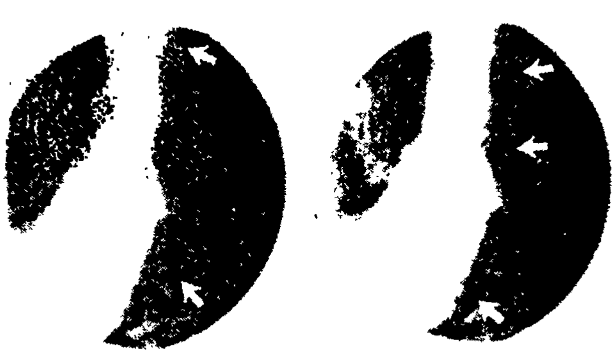

Fig. 2.—Spot film of irregularity of greater curvature of stomach, showing ulceration.

cells within the layer without careful search. The search, however, reveals occasional atypical epithelial cells, some of which resemble signet ring cells. Signet ring cells are prominent within the mucosa. Several overlying erosions and ulcerations are noted. These are not prominent. Examination of all lymph nodes fails to reveal evidence of metastatic neoplasm. At no point is there an attempt to form glands or papillary structures. The strip of proximal gastric wall fails to reveal evidence of neoplastic cells. The diagnosis is linitis plastica.

Comment

Linitis plastica occurs infrequently, and in recent years very few cases have been recorded in the English literature. There have been varying opinions about whether linitis plastica can always be considered to be a malignant lesion. The Quarterly Cumulative Index Medicus, for instance, records this disease under "gastritis" and also under "stomach neoplasm," indicating that the classification of this disease needs further clarification.

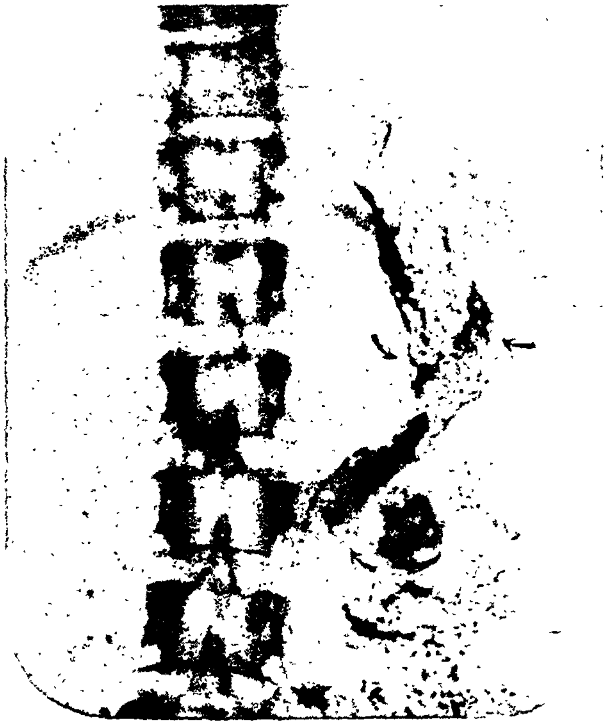

Fig. 3.—Mucosal studies of stomach: note abrupt ending of parallel folds in upper portion of stomach. In region of the defect, mucosa is irregular. Normal folds are again visible in antrum. Comparing figures 1 and 3, note that greater curvature is not entirely rigid.

The roentgenographic signs of linitis plastica are due to a fibrous infiltration, with development of excessive connective tissue in the gastric wall. According to Bockus,[1] not all cases of linitis plastica are due to carcinoma. Among other known causes for this pathology are gastric syphilis, tuberculosis, and an "innate fibrous tissue diathesis." This possibility is suggested by the occasionally associated occurrence of diffuse fibrosis in other organs: e. g., fibrotic lesions have been found in the intestinal tract, gallbladder, and more rarely in other abdominal organs. Perhaps these lesions may be regarded as examples of abdominal keloid. A more plausible explanation for marked proliferation of the fibrous tissue in linitis plastica is the presence of an irritant of low virulence, acting continuously and slowly over a long period.

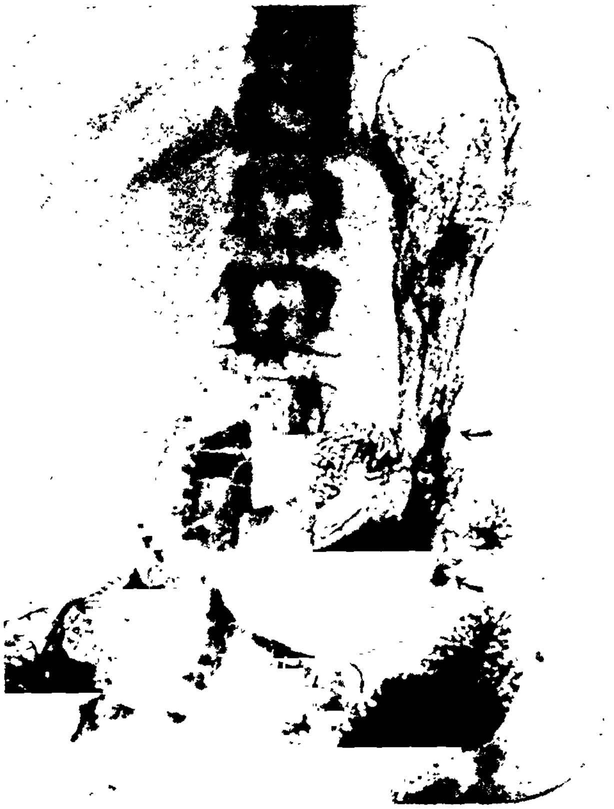

Fig. 4.—Mucosa of stomach six months before operation: note abrupt ending of parallel folds in middle of stomach. Mucosa of greater curvature below this margin shows less pronounced irregularity than that in figure 2.

Evidently the type of carcinoma often responsible for linitis plastica is of low virulence and slow growth, so that the connective tissue proliferation more than keeps pace with multiplication of cancer cells. In benign lesions the same theory may be applied, the toxin being continuously elaborated but never sufficiently lethal to cause the development of an inflammatory granuloma. A third possible mechanism for benign linitis plastica is suggested by the case of DeTakats showing resolution after acute diffuse suppurative inflammation of the stomach.[1] Teschendorf[2] is of the opinion that benign infiltration of the stomach wall may undergo malignant degeneration. Gigli,[3] on the other hand, does not believe that linitis plastica should be considered an entity with constant characteristics caused by a particular type of neoplasm or by an inflammatory process. The term linitis plastica should be used to express a particular histological picture in which hypertrophy of the connective and muscular tissues is seen. The cause of this condition is nearly always an infiltrating type of carcinoma, but it may be another type of tumor or, more rarely, an inflammatory process.

Rigler and co-workers [4] have described an eosinophilic granuloma which simulates the roentgenographic changes seen in linitis plastica. Teschendorf [2] states that the roentgenographic differential diagnosis is difficult because linitis plastica simulates scirrhous carcinoma. Buckstein [5] reports a case of linitis plastica with an infiltrative, scirrhous-type new growth. In his case, there was roentgenographically an abrupt termination at the border of the pathology.

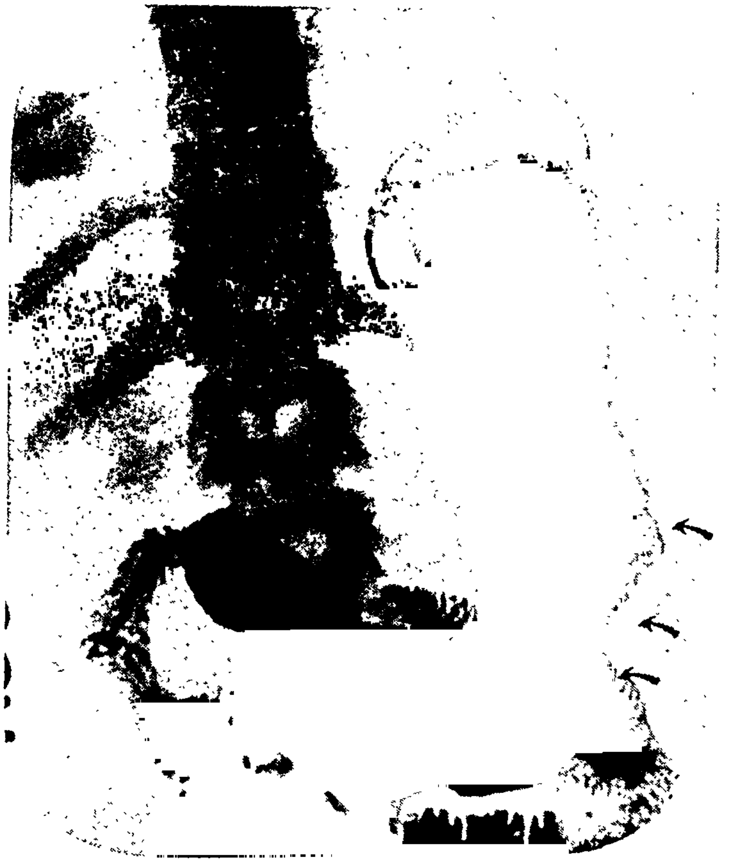

Fig. 5.—Roentgenogram of stomach six months before operation, showing irregularity of greater curvature of stomach.

The roentgenographic signs of this disease are due to the infiltrative process in the gastric wall.[6] We find, therefore, a loss of elasticity in this region, usually on the greater curvature. Generally, it appears as if the curvature were straightened. Definite masses are rarely visualized. In most instances, the lesion starts at the pylorus and progresses orally. The narrow rigid antrum and the normal corpus of the stomach cause the characteristic appearance which has been described as a "leather-bottle" stomach. Our case is similar to that of Buckstein,[5] since it did not involve the antrum of the stomach. Typical of the "leather-bottle" stomach is that the duodenal cap, never being involved, seems to be much larger than the antrum of the stomach, making this section appear like a mushroom with a narrow stem.

Of greatest importance in establishing the roentgenographic diagnosis is the study of the gastric mucosa by a thin layer of contrast substance. This can be seen only on a film, not during fluoroscopy. The changes are so minute that only a film can reveal the pathology. To our knowledge, the mucosal changes in linitis plastica have not been previously demonstrated and described. The mucosal studies reveal an irregular surface, without typical carcinomatous changes. They show, however, the delineation between the normal and the diseased area. Excessive mucus, which is occasionally present in the stomach (even in a fasting stage) may impair the roentgenographic studies. In such cases reexamination is indicated. Diagnosis and interpretation of the findings are only acceptable if the same mucosal changes are reproduced on two independent examinations, as was done in this instance.

Summary

In a 44-year-old woman, who had a proved case of linitis plastica, the clinical symptoms extended over a period of three years and consisted of epigastrial pains and heartburn, clinically simulating a peptic ulcer. Roentgenographic examination revealed the presence of an early infiltrating linitis plastica with an ulceration, which was verified by operation. We wish to stress that roentgenographic studies of the gastric mucosa are of utmost importance in diagnosing linitis plastica. These studies reveal the extent of the disease. Linitis plastica, in its beginning stages, roentgenologically shows some flexibility of the gastric wall and is therefore distinguishable from other forms of carcinoma, in which constant rigidity of the stomach wall is observed. To our knowledge, early cases of linitis plastica have not been reported heretofore. This proved case did not reveal the roentgenographic findings of a typical "leather-bottle" stomach.

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VALIDITY OF PATHOLOGICAL DIAGNOSIS OF BREAST CANCER

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and
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The reliability of the diagnosis of cancer was questioned in connection with a series of cases of mammary carcinoma in which the five-year survival rate, among patients in whom the diagnosis had been confirmed by histopathological study, had been 44%. Slides representing 136 such cases were reviewed independently by three pathologists. In 130 of the 136 cases their reports were either unanimously positive or unanimously negative as to the diagnosis of cancer. It was necessary to conclude that the histopathological examination had a high degree of reliability and that the five-year survival rate found in this series of mammary carcinomas was genuine.

Underlying discussions on the survival experience of cancer patients there is often a certain degree of doubt whether all the cases actually were cancer. In discussing a report on the survival experience of patients with breast cancer in one of the hospitals participating in the California Tumor Registry, Dr. L. Henry Garland of San Francisco voiced this doubt. He expressed the opinion that the survival rate for breast cancer given in the registry might be too high because of inclusion of cases that were not actually cancer. The decision to undertake this study of the validity of diagnosis of breast cancer was a result of that discussion.

Purpose of Study

The California Tumor Registry is a central registry of 38 hospitals in California that is operated by the Bureau of Chronic Diseases, California State Department of Public Health. The registry receives abstracts of 17,000 cancer cases per year, an estimated one-third of the cancer cases newly diagnosed in the state each year. It has a total of over 200,000 cases in its files, beginning with cases reported in 1942, with an annual follow-up of patients that is 91% complete.

The report given at the meeting referred to above disclosed a 44% five-year survival rate for patients with breast cancer whose cases were initially diagnosed in hospitals reporting to the registry between 1942 and 1948. This survival rate is similar to the five-year survival rate found in other medical facilities and registries: University of California,[1] 1918-1947, 40.4%; Connecticut,[2] 1941-1946, 47.0%; and Johns Hopkins,[3] 1941-1945, 36.7%.

It was also reported at this meeting that more than 85% of all the 1942-1948 cases of breast cancer in the California Tumor Registry had been reported as histopathologically confirmed and that the percentage of confirmed cases has been increasing over the years, reaching 93.4% in 1956.

The validity of the diagnoses of breast cancer in the California Tumor Registry was then questioned on the basis of the premise that the microscopic diagnoses may have been incorrect, with a tendency for pathologists to report cancer when it did not exist. If this were true, it would result in a survival rate for cancer patients that is deceptively higher than it really is.

As a result of this discussion, the Tumor Registry Advisory Committee (appointed by the California Medical Association) recommended that the Cancer Commission of the California Medical Association, the California Society of Pathologists, and the California Tumor Registry jointly undertake a study of validity of pathological diagnoses in registered patients with breast cancer who survived five years or more. It was proposed that the original slides for a sample of cases be obtained and then be independently reviewed by three outstanding pathologists, each pathologist to review the slide and state whether the diagnosis was "cancer" or "not cancer." Disagreements were to be resolved by majority opinion.

Selection of Sample Cases for Study

The study was based on the 1942-1948 cases of breast cancer reported to the California Tumor Registry in which the original diagnoses had been confirmed by histopathological studies. The registry included 1,550 such cases of patients with at least five-year survival and, of these, 1,452 had been confirmed histopathologically.

Since investigation of all 1,452 cases was considered too laborious, it was estimated that a 10% random sample would provide a satisfactory degree of reliability. Each of the 1,452 cases was represented by an IBM tabulating card. A table of random numbers was used to preclude bias in determining which of the first 10 cards would be

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From the Bureau of Chronic Diseases, California State Department of Public Health (Chief, Dr. Breslow, and Mr. Linden), and the Cancer Commission, California Medical Association (Drs. Cline, Wood, and Guiss).

psychosis" being listed as the cause of death on the death certificate. A second patient, admitted and treated for breast cancer (a positive biopsy specimen having been obtained) in another hospital in the California Tumor Registry system two years after her original diagnosis, died during the sixth year after original diagnosis, with the following statement on her death certificate: "Ca. of breast with metastasis, arteriolar nephrosclerosis, uremia."

Confirmed vs. Unconfirmed Cases.—Although the present study included confirmed cases only, the over-all survival rate of 44% of patients for the period 1942-1948 was based on all cases, both those confirmed histopathologically and those not so confirmed. To determine whether the survival figure was possibly affected by the inclusion of cases without microscopic confirmation, five-year survival rates were obtained for patients with confirmed and unconfirmed cases, by stage of disease at the time of diagnosis.

The five-year survival rate for patients with confirmed cases is 48.3% as contrasted with 18.9% for unconfirmed cases. The higher survival rate for patients with confirmed cases is maintained at each stage of the disease. It is clear that the over-all 44% survival rate can not be challenged as being too high because of the inclusion of unconfirmed cases. Exclusion of the unconfirmed cases would make the survival rate higher than 44%.

TABLE 7.—*Five-year Survival Rates for Patients with Confirmed and Unconfirmed Cases of Breast Cancer, for Each Stage of Disease*

	Five-year Survival, %	
Stage	Confirmed	Not Confirmed
Localized	70.3	(28.0)*
Regional	41.1	17.6
Distant metastasis	28.9	6.0
Not recorded	56.7	32.2
Total cases	48.3	18.9

*Based on less than 50 cases.

Summary and Conclusions

This study was undertaken to test the validity of microscopic diagnosis of breast cancer reported to the California Tumor Registry in patients who had survived at least five years. Specifically, the study valuated the five-year survival rate of 44% of patients whose cases had been diagnosed during the period 1942-1948.

In a sense, the method used in this study does not measure the true validity of the microscopic diagnoses. Such determination would have to be arrived at by comparing the original diagnoses with some independent proof of cancer. In this study, the original diagnoses are compared with the diagnoses made independently by three outstanding pathologists. Such a comparison is considered the best available "proof" of cancer.

The first review by the three pathologists yielded a majority decision of "cancer" for more than 90% of the cases. A second review of additional slides for some of the cases diagnosed as "not cancer" by the reviewing pathologists brought the percentage confirmed to 95.6%. Death certificate information indicates that two of the six remaining patients also had cancer of the breast.

The present study was based on histopathologically confirmed cases in patients with at least five years of survival. The other portions of the total breast cancer group must be considered in evaluating the survival rate for all the patients with breast cancer. Inclusion of the unconfirmed cases, as shown in table 7, could not have made the survival rate too high, and there can be little doubt about the malignancy of the vast majority of cases in patients who did not survive five years. It appears, therefore, that the five-year survival rate of 44% of patients whose cases were reported to the California Tumor Registry during 1942 to 1948 is validly based on cases of malignant breast cancer. Although the results refer to cases diagnosed during the years 1942-1948, it seems reasonable to assume that the quality of microscopic diagnosis of breast cancer has remained at the level found in the study or even improved in recent years.

Can it be assumed that the findings of this study also describe the level of microscopic diagnosis for all cases of breast cancer in California? The California Tumor Registry is based on about one-third of all general hospital beds in the state located in hospitals with 50 beds or more, including teaching and nonteaching, public and private, urban and rural, and large and small hospitals. Comparison of the hospitals participating in the registry with all general hospitals in the state with regard to size of hospital, geographic distribution, and distribution of cancer deaths by site of cancer indicates that hospitals listed in the registry are generally typical of hospitals in the state. It would thus appear that the level of accuracy in microscopic diagnosis of cases of breast cancer found in this study prevails throughout the state.

The findings are indicative of the quality of diagnosis afforded to patients with breast cancer. Proposals have now been made for similar studies on other sites and types of cancer, such as cancer of the thyroid, in situ cancer of the cervix and lymphosarcoma.

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The Cancer Commission of the California Medical Association, the California Society of Pathologists, and the California Tumor Registry of the California State Department of Public Health express their appreciation to the three reviewing pathologists, Drs. Alvin J. Cox, Stanford University, Hugh A. Edmondson, University of Southern California, and Henry D. Moon, University of California, for their cooperation in the study and thank the hospitals participating in the study for making their slides available.

The Tumor Registry Advisory Committee is appointed by the California Medical Association and consists of Drs. John W. Cline, David A. Wood, and Lewis W. Guiss; Dr. Walter E. Batchelder, acts as secretary.

Miss Jo Ann Wray assisted in the preparation of this study.

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PREVENTION OF PSYCHIATRIC HOSPITALIZATION WITH USE OF PSYCHOPHARMACOLOGICAL AGENTS

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The effectiveness of promazine hydrochloride or chlorpromazine hydrochloride in preventing psychiatric hospitalization was studied in 173 schizophrenic outpatients. Pharmacological therapy was given, with brief psychiatric interviews. The two drug groups consisted of 55 patients receiving promazine and 62 who received chlorpromazine; the comparison group of 56 patients received a placebo under double-blind conditions. The treating psychiatrist did not know which of the three substances the patients in a given group were receiving, but he was free to adjust dosage in an effort to achieve results. The two groups receiving the ataractic drugs had a significantly lower rate of subsequent hospitalization than did the group receiving the placebo. The placebo was prescribed in significantly greater amounts than the ataraxics, apparently reflecting the psychiatrist's effort to achieve results.

The dramatic effects and the value of ataractic agents in psychiatric treatment have by now become a clinically accepted fact. It remains for psychopharmacological research to validate the broad lines laid down by clinical findings. One major area in need of objective validation is the effect of therapy with ataractic drugs on the hospitalization rate among psychiatric patients prone to breakdown. It is obviously of great importance whether the new drugs are able to reduce the hospitalization rate among patients with the major psychiatric illnesses. Although several clinical and statistical reports claim that ataractic treatment prevents hospitalization, a review of the literature fails to reveal a controlled study verifying this proposition.

There are, however, considerable difficulties in evaluating and proving such a drug effect. It is well known, for example, that a new treatment may produce a wave of enthusiasm which may affect clinical outcome beyond the specific medication effect. In a recent study of inpatient treatment, Linn[1] observed considerable change in hospital release rates after introduction of therapy with ataractic drugs, although the effects were generally no greater among patients treated with medication than with placebo. He concluded that "staff optimism" may have been the pivotal force in the higher release rates. Furthermore, he noted that "patients who were continued on maintenance dosages of chlorpromazine and reserpine into the release period were not any more likely to stay in the community for a year than patients not so continued."[1]

In the present study we have approached the investigation of the effect on hospitalization rate of ataractic treatment by assigning drug and placebo treatment on a random basis to equivalent patient groups and administering the treatment under double-blind conditions.

Materials and Method

One hundred seventy-three schizophrenic outpatients were given medication in the context of brief psychiatric interviews for periods up to 18 months. The medicament was in the form of pink capsules containing either placebo, promazine hydrochloride, or chlorpromazine hydrochloride and

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supplied to the psychiatrist in single-strength and double-strength doses corresponding to 50 and 100 mg., respectively, of the active agents. Drug assignment was random. The treating psychiatrist did not know which agent the patient received, although he did know the possible contents. He was free to vary the dose as his clinical judgment dictated.

The patients in the study were selected on the basis of the following criteria: (1) age, 18 to 40 years; (2) evidence of schizophrenic illness existing for over one year prior to clinic admission; (3) willingness to accept drug treatment; and (4) the presence of a cooperative, English-speaking relative.

Findings

Of the total 173 patients, 16.8% or 29 patients were hospitalized for mental illness during the course of treatment. Hospitalization usually involved certification to a state hospital (25 of 29 patients). When an analysis according to treatment agent was made, a clear distinction was seen between the rate of hospitalization for the placebo group and for the active treatment groups. As shown in the table, 28.6% of the placebo patients were hospitalized, while 18.2% and 4.8% of the promazine and chlorpromazine groups, respectively, were hospitalized. The differences are statistically significant at the 0.01 level of probability ($\chi^2=11.97$; 2 degrees of freedom).

*Clinical Outcome of Treatment, According to Psychopharmacological Agent Used, in 173 Schizophrenic Outpatients**

	Type of Treatment							
	Placebo		Promazine		Chlorpromazine		Total	
Clinical Outcome in Patients	No.	%	No.	%	No.	%	No.	%
Hospitalized	16	28.6	10	18.2	3	4.8	29	16.8
Nonhospitalized	40	71.4	45	81.8	59	95.2	144	83.2
Total	56	100.0	55	100.0	62	100.0	173	100.0

* $\chi^2 = 11.97$; $p < 0.01$.

As a further test of the validity of the findings, a number of variables along with specific treatment were considered. Our first consideration was a comparison of the specific treatment effects when the treatment groups were matched for prognostic features. This step was necessary because of the possibility that the over-all treatment groups were unequal prognostically and that the effect seen was a result of the type of patient within the treatment group rather than of the specific treatment. Three criteria will be considered in comparing the patients in the three drug groups: (1) history of psychiatric hospitalization, (2) history of commitment, and (3) severity of illness ratings. In addition, the treatment groups were studied in terms of dosage used and drop-out rates.

History of Psychiatric Hospitalization.—From among the total 173 patients, all those patients were selected who had undergone any form of psychiatric hospitalization for any length of time. It was found that 138 of the patients had had some form of psychiatric hospital experience. This group of patients was then divided according to treatment type, and the rate of hospitalization during treatment was obtained. The trend of a lowered rate of hospitalization with use of the specific agents as opposed to the placebo was again noted: 31.1% for placebo; 22.2% for promazine, and 4.2% for chlorpromazine ($\chi^2= 11.57$; $p < 0.01$).

History of Commitment.—Eighty patients who had a history of commitment to a state hospital were considered next. Seventeen of these 80 underwent rehospitalization during treatment. An analysis according to treatment agent revealed the trend of a reduced rate of hospitalization among those patients treated with chlorpromazine: 28.1% for placebo; 29.2% for promazine, and 4.2% for chlorpromazine ($\chi^2 = 5.98$; $p = 0.05$).

Severity of Illness Ratings.—At the initial interview the psychiatrist rated the patient in terms of over-all severity of illness. This rating, which represents a quantification of global clinical impression, has been found by us to be highly correlated with a morbidity index derived from a detailed psychiatric evaluation scale, adapted from the Lorr Scale.[2] The over-all or global severity rating was used in the present study because of its simplicity and high correlation with the detailed morbidity index.

With use of the over-all rating, those patients considered "severly ill" were studied. This included 114 patients, 22 of whom were hospitalized. An analysis according to treatment confirmed the greater potency of the ataractic drugs over placebo in preventing hospitalization, with rates of 31.6% for placebo, 23.5% for promazine, and 4.8% for chlorpromazine ($\chi^2= 9.76$; $p < 0.01$).

Dosage Level.—A final variable to be considered was the specificity of usage or dosage of the agents. As mentioned, the psychiatrists were free to vary the dosage, and a considerable range was used. By studying the complete medication record of each patient, a "modal dosage" or number of drug units per day most frequently prescribed by the psychiatrist was determined. A drug unit is equal to 50 mg. of active agent. The range of modal dosage was from 1 to 16 units (for active agent, 50 to 800 mg.) per day. An examination of the modal dosages for the three agents revealed a much greater use of higher dosages for the placebo than the active agent. By designating 5 or more drug units per day (250 mg. or more of active agent) as a "high" modal dosage, it was found that 50% of the patients in the placebo group received such dosage, while 23.6% and 16.1% of the patients receiving promazine and chlorpromazine, respectively, were on the "high" modal dosage. Thus, the placebo was clearly used in a different manner from the active agent.

As a gauge of dosage effectiveness, the rate of hospitalization with "high" and "low" modal dosage was determined for the placebo and active agent groups. (Because of the small number of cases in these subgroups and the infrequent use of chlorpromazine in high dosage, the two ataractic groups were collapsed in the analysis of data.) With "low" dosage, the placebo group had a hospitalization rate of 21.4% (6 of 28 patients), while the ataractic series was 11.7% (11 of 94 patients). When the "high" modal dosage was given, the placebo series hospitalization rate rose to 35.7% (10 of 28 patients), while the ataractic rate fell slightly to 8.7% (2 of 23 patients). Thus, it appears that when the psychiatrist perceived a need for and prescribed higher doses, the effect of ataractic treatment became more striking: increased dosage of placebo was associated with greater incidence of hospitalization, whereas use of increased doses of active agents continued to result in a lowered hospitalization rate.

Spontaneous Drop-Out.—As a further consideration of over-all treatment effects, that large segment of patients who spontaneously dropped out of treatment, for reasons other than hospitalization, was studied according to the treatment agent. No significant differences were observed among the three agents for spontaneous drop-out. The over-all drop-out rate was 36.4% (63 of 173 patients), while for the individual agents the rates were as follows: placebo, 33.9%; promazine, 34.5%; and chlorpromazine, 40.3%.

Summary and Conclusions

This study attempted an objective validation of the claim that the ataractic treatment of psychiatric outpatients prevents hospitalization. The method involved random assignment of drug and placebo treatment to equivalent patient groups with drugs administered under double-blind conditions. Ataractic treatment was associated with significantly lower rates of hospitalization than placebo usage. The lowered rate of hospitalization was observed when the subgroups were equated on the basis of past hospitalization history and severity of illness. When the treating psychiatrists increased dosage levels in response to clinical conditions, the effect of ataractic drugs in reducing the rate of hospitalization was accentuated.

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MULTIPLE SCLEROSIS, RHEUMATIC FEVER, AND ALLERGY.—The view is becoming prevalent that "multiple sclerosis," as now used, refers to a group of diseases which ultimately will be found to be of diverse etiologies. The speculations . . . on allergic mechanisms, must be understood, therefore to apply only to a portion, great or small, of multiple sclerosis patients. . . . Some clinical characteristics of multiple sclerosis are reminiscent of rheumatic fever. Both illnesses are characterized by transient attacks which may or may not leave permanent tissue damage. Both are common in cold climates and uncommon in tropical ones. There is a familial incidence of both diseases although this is apparently more uniform in rheumatic fever than in multiple sclerosis. Both illnesses have been ascribed to a hypersensitivity reaction. For rheumatic fever, this hypothesis has been fairly generally accepted on evidence of its close clinical relations with streptococcal infection, and the immunological responses of the rheumatic fever patient to streptococcal products. The thesis that some [form of] multiple sclerosis is the manifestation of an allergic reaction of the nervous system is based on . . . [the following] data: 1. Analogy of rapidly appearing and disappearing signs and symptoms with similarly rapidly altering allergic phenomena. 2. Cases of transient and sometimes severe neurological signs and symptoms following exposure to allergens, usually food allergens. 3. Fairly high incidence, in the serum of multiple sclerosis patients, of positive complement fixation reactions to antigen derived from brain and spinal cord of multiple sclerosis occurring with significant frequency during or immediately following acute allergic episodes. 4. The existence of a demyelinating disease, presumably allergic in nature, produced in several species of animals, by using as antigen brain and spinal cord emulsion treated with . . . [an] adjuvant.—D. K. Ziegler, M.D., Multiple Sclerosis and Rheumatic Fever: Related Diseases, *Diseases of the Nervous System,* May, 1959.

TUBEROUS SCLEROSIS COMPLEX

UNUSUAL CASE OF ADENOMA SEBACEUM, TUBEROUS SCLEROSIS, AND EXTENSIVE BONE LESIONS

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and
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A patient who came for treatment of a conspicuous facial skin lesion gave evidence of impaired mentality and a history of epilepsy. Roentgenographic examination yielded evidence of extensive osseous lesions of the vertebral column and pelvis, including bilateral congenitally dislocated hips. The cutaneous lesion was an adenoma sebaceum. The finding of a lesion of this kind in a patient warrants a complete bone survey.

The recent literature indicates that adenoma sebaceum must now be added to the lengthening list of dermatological conditions in which a complete bone survey is indicated. Although this disease has long been known to be associated with visceral lesions, the occurrence of skeletal changes has been appreciated only in recent years. Its occurrence in the spinal column was noted in 1957 by Beck and Hammond [1] and Ashby and Ramage.[2] The present report concerns a patient with adenoma sebaceum and tuberous sclerosis associated with extensive bone changes in the spine and pelvis as well as the calvarium.

Brain lesions in this disease and a rhabdomyoma of the heart were described by Von Recklinghausen [3] as early as 1863, but the name, tuberous sclerosis, was given to it by Bourneville [4] in 1880. It is of interest that Bourneville's patient had "acné rosacée et pustuleuse de la face; de plus éruption vésiculo-papuleuse confluente du nez, des joues, du front; — nombreux petits molluscums à la nuque et sur les parties du cou." Although Balzer and Menetrier [5] in 1885 described a young woman with adenoma sebaceum, she was apparently neither epileptic nor mentally deficient. In 1890 Pringle [6] published his classic description of adenoma sebaceum in a 25-year-old woman who was of low intelligence. It was not until 1908, however, that Vogt [7] postulated the now classic triad of adenoma sebaceum, mental deficiency, and epilepsy, as well as the occurrence of renal and cardiac tumors, as a unit disease. The familial propensity of this disease was subsequently noted by Berg [8] in three generations of a family. The oldest member of the family, a man, died at the age of 66 years as a result of a tumor of the left kidney. His son, who had adenoma sebaceum, epilepsy, and a right-sided renal tumor, died at the age of 28 years after operation. His granddaughter died at the age of 8 years, carrying the stigmata of mental deficiency, adenoma sebaceum, and a small left-sided renal tumor.

With the development of radiology, the intracranial calcifications of tuberous sclerosis became detectible in life, but bone lesions in the calvarium, hands, and feet were not reported until 1935 by Gottlieb and Lavine,[9] and later by Dalsgaard-Nielsen.[10] Numerous reports have since substantiated the radiographic findings in the calvarium, hands, and feet. Ackermann,[11] Budenz,[12] and Lucas and Davis [13] noted sclerotic areas in the ribs and pelvis, but their patients with tuberous sclerosis had no skin changes suggestive of adenoma sebaceum. In 1957 Beck and Hammond [1] and Ashby and Ramage [2] almost simultaneously reported extensive bone changes in the spine and in the pelvis in addition to those in the calvarium and phalanges in patients with tuberous sclerosis. Whitaker [14] subsequently detected these skeletal changes in one of three cases.

Report of a Case

A 27-year-old woman was first seen in the Dermatology Clinic of Northwestern University Medical Center on March 26, 1959, requesting treatment of a "birthmark" on the right infraorbital area which had been present since birth. She had been treated for epileptic convulsions from 1948 to 1950, and the lesion on the right cheek had been called a "birthmark" and a "cavernous hemangioma." Both parents and one sibling were in good health, but no direct examinations of them could be arranged.

The patient had a 4 by 8 cm. tan-colored, slightly elevated, irregularly shaped lesion in the right infraorbital area. The mass contained numerous hair-like keratinous follicular plugs. The nasal and malar skin showed numerous symmetrical papules with areas of hemangiomatosis (telangiectasia) (fig. 1 and 2). The posterior aspect of the trunk exhibited scattered papules measuring 0.5 to 2.0 cm. in diameter which were firm, pale, and nontender. No café au lait spots or shagreen skin were present. There was a subungual verruca vulgaris of the left thumb; however, no typical subungual fibroma as has been described in cases of tuberous sclerosis was found. On ophthalmoscopic examination of the retina a white plaque was visible at the medio-inferior margin of the right optic disk. Psycho-

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metric studies revealed the patient's mental level to be equivalent to that of a 7-year-old child (full-scale I. Q. of 44).

A faint trace of albumin was detected in the urine on two occasions but none was found on the third examination. Results of tests for sugar were negative. The sediment showed only occasional white blood cells and hyaline casts. Results of the Kahn and Wasserman tests, blood counts, and a three-hour glucose tolerance test were normal, as were the electrocardiogram and chest x-ray. An intravenous pyelogram failed to show any demonstrable kidney abnormalities.

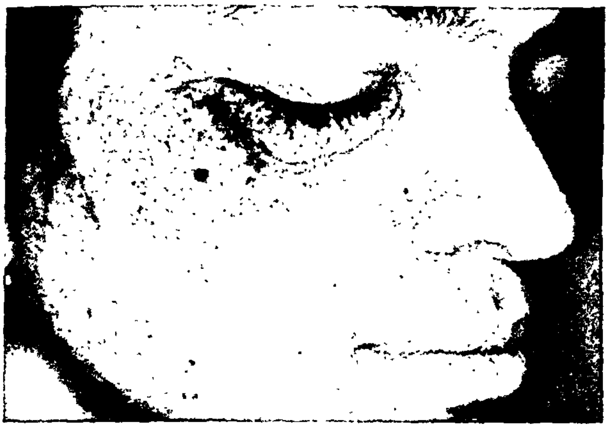

Fig. 1.—View of right side of face showing numerous tiny papules and large pigmented elevated lesion in malar and infraorbital area.

Roentgenographic studies revealed widespread aberrations of the bones. There were extensive focal and confluent sclerotic lesions involving individual vertebral segments from the atlas through the sacrum. The posterior elements of the neural arch as well as the bodies of the vertebrae were affected (fig. 3). These lesions extended into the lower ribs on each side and into the pelvic bones. Bilateral congenitally dislocated hips, with the formation of false acetabular cavities, could be detected easily. The upper portion of the shaft of the right femur showed amorphous sclerotic changes which were thought to be similar to the other areas (fig. 4). Within the skull numerous calcified deposits were visible; in addition, the inner table of the frontal bone exhibited the sclerotic changes described by Gottlieb and Lavine[9] (fig. 5). There were no areas of rarefaction, cyst-like changes, or cortical fragmentation. Roentgenograms of the hands and feet showed no abnormalities.

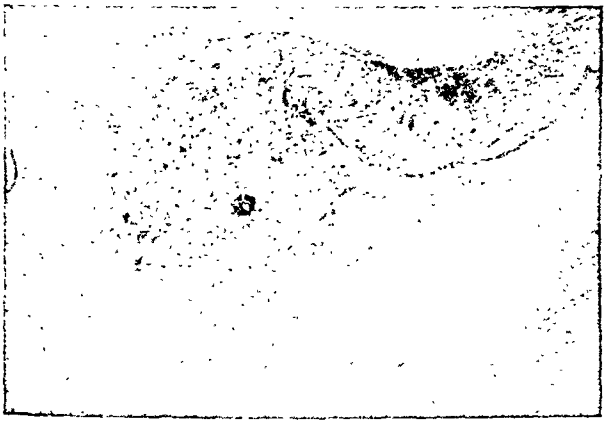

Fig. 2.—Enlarged view of right malar and infraorbital area shown in figure 1.

Microscopic examination of tissue sections from the right infraorbital lesion showed the epidermis to be normal except for unusually heavy pigment in the region of the basal cell layer. The dermis exhibited numerous mature and immature hair follicles containing tiny hairs and fragmented keratin but no sebaceous glands. Tissue sections from a paranasal papule also showed normal epidermis but no increase in pigment. The dermis contained many small hair follicles and hypertrophied sebaceous glands. There was pronounced dilatation of blood vessels in the superficial corium, with a mild perivascular infiltrate of lymphocytes.

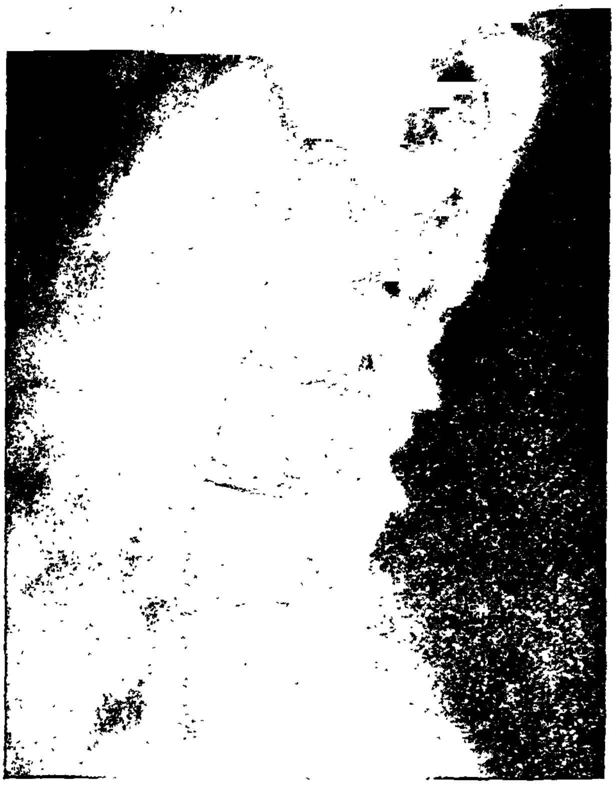

Fig. 3.—Lateral roentgenogram of lumbar region showing sclerotic changes in vertebral bodies, neural arches, and lower ribs.

Comment

Bone lesions as a concomitant finding in adenoma sebaceum have not been emphasized in the standard textbooks on dermatology. Berland[15] and

Holt and Dickerson[16] noted that about 65% of patients with tuberous sclerosis have changes in the bones of the hands and feet which are detectible by roentgenographic examination. The presence of intracranial calcifications or sclerosis of the skull raised the possibility of radiographic detection to 85%. It has been estimated that about 50% of those with tuberous sclerosis have no skin lesions of adenoma sebaceum. No direct percentage relationship between adenoma sebaceum and bone lesions has been mentioned in the literature, and such estimates are difficult to obtain from published case reports. The relatively rare occurrence of spinal and pelvic bone lesions in adenoma sebaceum as compared to the bone lesions in the acral parts may well reflect a lack of awareness of this possibility.

The occurrence of lesions in all parts of the skeletal system as well as in the kidney, heart, lung, liver, spleen, eye, and brain is not unexpected when one considers adenoma sebaceum as but one facet of a broad neuroectodermal disease,[17] or disseminated hamartiosis.[18] Under these concepts the three diseases, multiple neurofibromatosis, encephalotrigeminal angiomatosis (Sturge-Weber), and the tuberous sclerosis complex, and possibly a fourth—hemangioblastomatosis (Lindau)—would represent disseminated defects or hamartomas. Combinations of these conditions have occurred with moderate frequency. Lesions of the spine and pelvis in association with multiple neurofibromatosis have long been recognized, and it is not surprising therefore that they should occur in the tuberous sclerosis complex. Their incidence in adenoma sebaceum can only be determined by a complete bone survey in all patients with this condition.

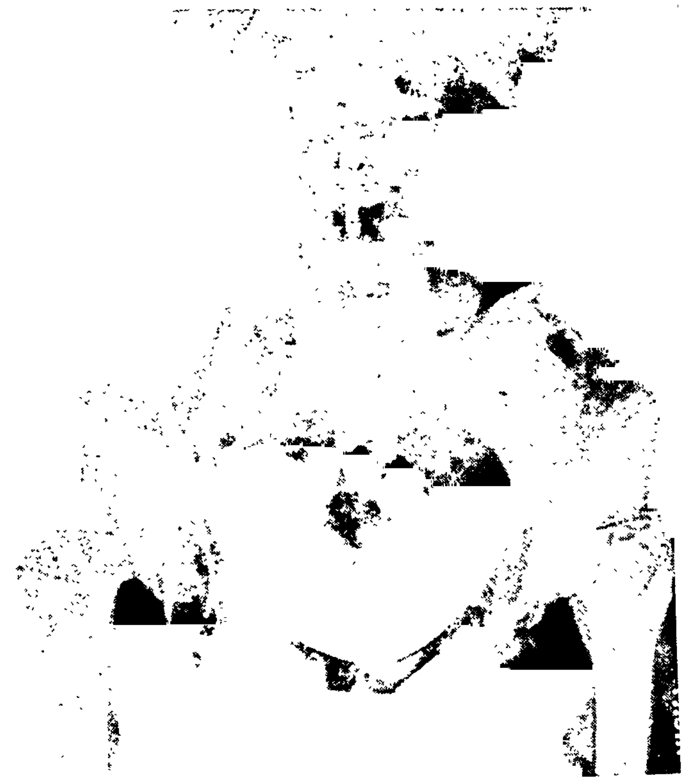

Fig. 4.—Roentgenogram showing bilateral congenitally dislocated hips, with formation of false acetabular cavities; focal and confluent sclerotic changes in lower ribs, lumbar vertebral bodies, sacrum, and iliac bones.

Summary

A patient, whose case is reported, had adenoma sebaceum, tuberous sclerosis (epilepsy and mental deficiency), and extensive bone lesions of the spine, pelvis, and calvarium. The frequency of bone lesions in the tuberous sclerosis complex warrants a complete bone survey in patients with adenoma sebaceum. Such bone surveys may show that spinal and pelvic lesions are not as rare as the literature indicates.

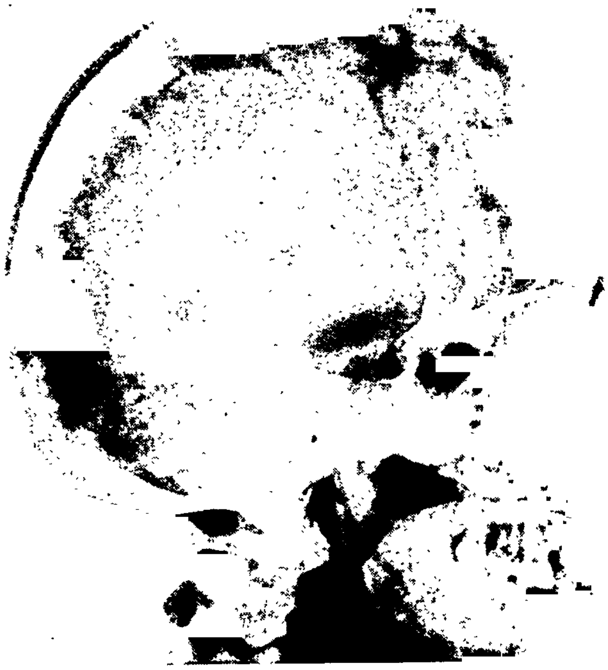

Fig. 5.—Lateral roentgenogram of skull showing calcified deposits within cranial cavity and sclerotic changes in calvarium.

303 E. Chicago Ave. (11) (Dr. Hasegawa).

Dr. H. J. Matthies, Department of Radiology, suggested performance of roentgenographic studies of the entire skeletal system after he had reviewed the skull roentgenograms.

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SIMULTANEOUS OCCURRENCE OF OSTEITIS DEFORMANS AND HODGKIN'S DISEASE

Arthur E. Davis Jr., M.D., Saint Cloud, Minn.

The possibility of finding osteitis deformans and Hodgkin's disease simultaneously in the same bone is illustrated in this case history of a 62-year-old man. Pain, persisting more than two weeks after an injury to the left knee, led to the discovery of osteitis deformans in the left tibia, and biopsy of an enlarged inguinal lymph node revealed malignant lymphoma. The patient died about four months after his admission to the hospital. At autopsy Hodgkin's disease was found in kidneys, spleen, liver, pancreas, thyroid, testes, and prostate; in addition it was found in the left tibia, sometimes in the same histological sections with areas of typical osteitis deformans.

The simultaneous occurrence of osteitis deformans (Paget's disease) and Hodgkin's disease in the same bone has not been described previously in the medical literature. The occurrence of osteitis deformans has been described in association with leprosy, hyperthyroidism,[1] giant cell tumors,[2] plasma cell (multiple) myeloma,[3] and trauma.[4] The French literature contains several cases associated with lymphatic leukemia.[5]

Osteitis deformans was first described by Paget[6] in 1877. The syndrome usually occurs in middle adult life, and there is occasionally a familial tendency.[7] The onset is insidious and the course is chronic. The bones most commonly affected are the skull, humerus, vertebral bodies, pelvis, femur, and tibia. When the disease is limited to a single bone, the tibia is the one most frequently involved.

The roentgenologic manifestations of osteitis deformans are reasonably characteristic. Porosis appears early. Later there is thickening and increased density, with complete or partial obliteration of the marrow cavities. There is coarsening and interweaving of the trabecular structures. A characteristic feature of tibial involvement is the persistence of a relatively normal pattern in the fibula, even when there is marked alteration in the tibia. The gross pathological characteristics are varied. In the earlier stages, the material is gray-pink and may be friable. Later, in long-standing processes, there is dense sclerotic bone.

The microscopic findings are characteristic: A typical mosaic pattern, with markedly thickened bone trabeculae, is seen. There are scalloped indentations. Both osteoblasts and osteoclasts are found. There is fibrovascular stroma between the t ened bone trabeculae. The dist

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Pathologist, Saint Cloud Hospital.

lines is seen in properly prepared sections. The fundamental disorder appears to begin as replacement of the marrow by fibrous tissue. While some bone trabeculae are being absorbed by osteoclasts, others are being thickened by osteoblasts. The end result is the thickened trabecular pattern, with the fibrovascular intervening stroma.

The cause of osteitis deformans is not known. The process is probably not a metabolic disorder, for it tends to be localized. Perhaps osteitis deformans represents a fundamental vascular disorder. In patients with advanced cases the blood flow through the involved bones may be up to 20 times normal. Work done by Storsteen and Janes[8] indicates that multiple small arterial venous fistulas probably are formed. The oxygen saturation of the arterial and venous blood also is increased in patients with advanced cases. A hyperemia of the overlying skin is often present. Other factors, such as trauma and stress, have been implicated in the disease, but no conclusive evidence has been presented.

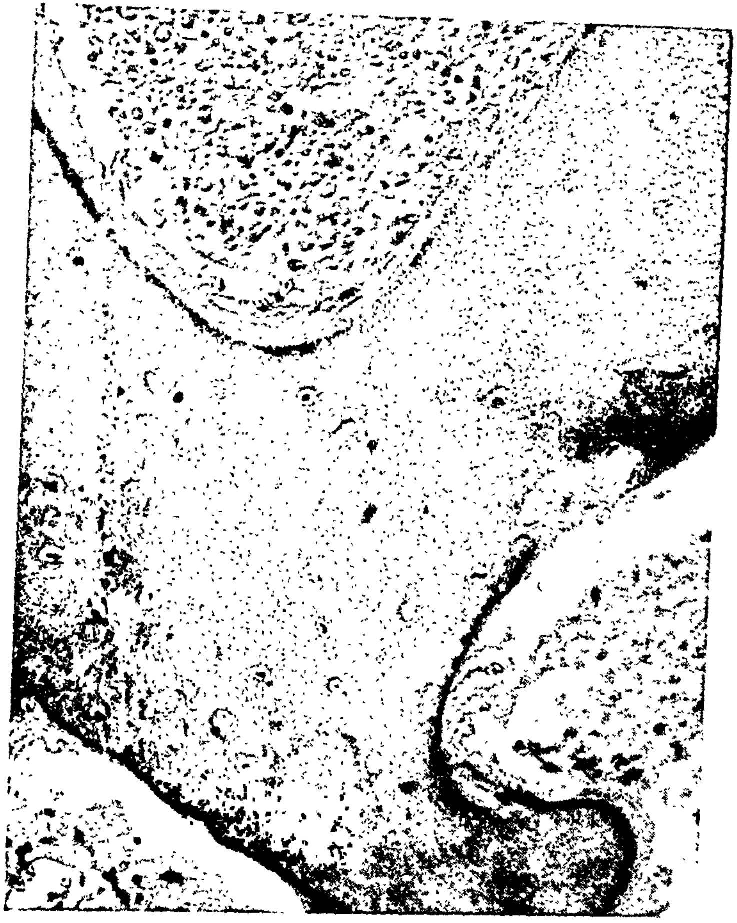

Fig. 1.—Photomicrograph of tibial biopsy specimen taken during life, showing Hodgkin's disease and osteitis deformans (Paget's disease); hematoxylin-eosin stain (× 110).

Hodgkin's disease is probably a fundamental disorder of the reticulum and is clearly a malignant process. Within a relatively short period the process tends to become generalized. Hodgkin's disease of the bone is common. Terminally, bone involvement is probably present in every case. The bone may be invaded directly from the invasive lymph nodes; however, most skeletal lesions are bloodborne metastatic deposits in the marrow.

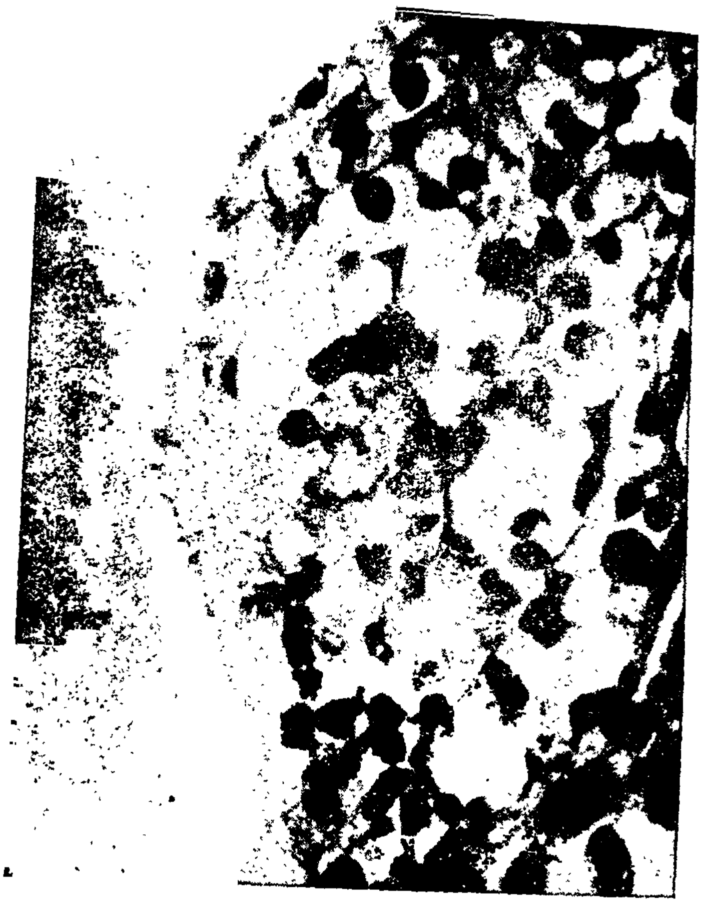

Fig. 2.—Hematoxylin-eosin stain (× 400) of specimen shown in fig. 1.

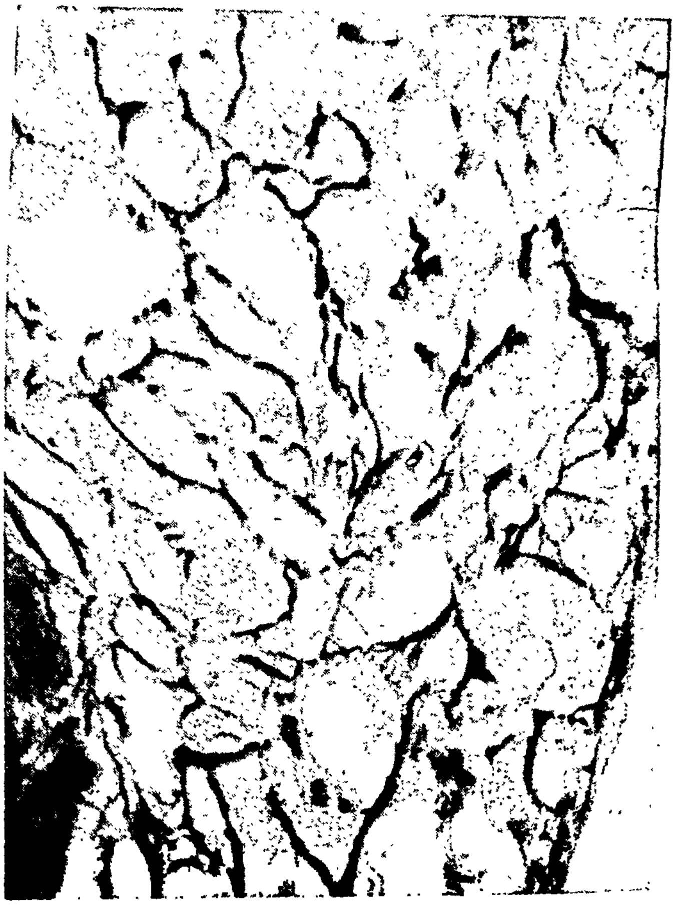

Fig. 3.—Reticulum stain of specimen shown in fig. 1 (× 400).

Considering the increased vascularity in osteitis deformans, it is unusual that more cases of association with malignancies have not been reported. The occurrence of metastatic carcinoma in association with osteitis deformans has been described. Osteogenic sarcoma develops in about 10% of the patients. The occurrence of fibrosarcoma and chondrosarcoma also has been reported. A historical study of osteitis deformans, with multiple sarcomatous transformations, was published in 1912.[9]

Report of a Case

A 62-year-old man struck his left knee while at work. The original pain persisted, became constant, and radiated to the toes. Two weeks later he consulted an orthopedic surgeon. Roentgenograms demonstrated osteitis deformans in the upper aspect of the tibia. Supportive measures were of little value. The pain increased in severity, and additional roentgenograms demonstrated increased sclerosis. A biopsy specimen demonstrated typical osteitis deformans.

Physical examination revealed tenderness over the left tibial tubercle that extended to above the knee joint. There was one+ pitting edema of the surrounding area that extended to the ankle. There was a small, palpable lymph node in the left inguinal region.

Laboratory Studies.—Results of serologic tests for syphilis were negative. The hemoglobin level was 12.7 Gm.%. The erythrocyte sedimentation rate was 74 mm. per hour. The white blood cell count and the differential count were within normal limits. The alkaline phosphatase level was 12 King-Armstrong units per 100 cc., the acid phosphatase level 1.5 Gutman units per 100 cc., the serum calcium level 10.5 mg.%, and the inorganic phosphorus level 3.2 mg.%. The total serum protein level was 6.6 Gm.%, 3 Gm.% albumin and 3.6 Gm.% globulin. Study of the urine revealed one+ albumin.

Roentgenographic Findings. — Roentgenograms of the upper aspect of the left tibia demonstrated a mottled sclerotic process involving the upper third of the tibia, with possible malignant changes.

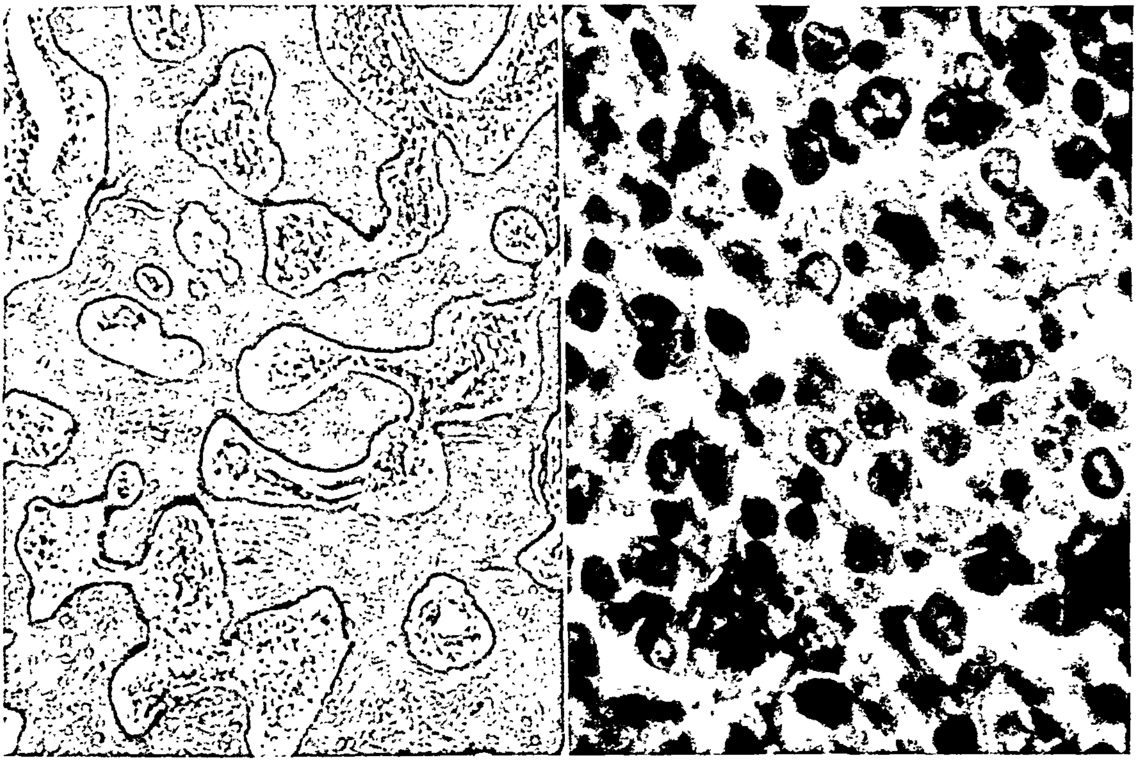

Fig. 4.—Photomicrographs of postmortem tibial biopsy specimen. *Left*, necrosis of intratrabecular substance: typical mosaic pattern of osteitis deformans persisting; hematoxylin-eosin stain (× 46). *Right*, retroperineal node: normal pattern replaced by sheets of atypical reticulum cells; hematoxylin-eosin stain (× 400).

Hospital Course.—The enlarged inguinal lymph node was removed, and microscopic studies revealed malignant lymphoma. Another biopsy specimen was then taken from the tibia to rule out malignant change. Sections taken at the second biopsy demonstrated changes in the bony pattern typical of osteitis deformans. The intertrabecular spaces, however, consisted of sheets of undifferentiated reticulum cells, instead of the usual fibrovascular stroma. Other sections of the tibia not involved by the lymphoma revealed typical osteitis deformans. The pathological diagnosis, at that time, was osteitis deformans and malignant lymphoblastoma involving the same histological sections (fig. 1, 2, and 3).

Lymphoma of the bone can produce a mosaic pattern similar to that found in osteitis deformans. This pattern is produced by simultaneous bone destruction and production. The gross and microscopic specimens were reviewed by Dr. David Dahlin of the Mayo Clinic, and the diagnosis of malignant lymphoma and osteitis deformans in the same histological section was confirmed. The findings of microradiograms performed at the Mayo Clinic were typical of osteitis deformans. A palpable abdominal mass developed.

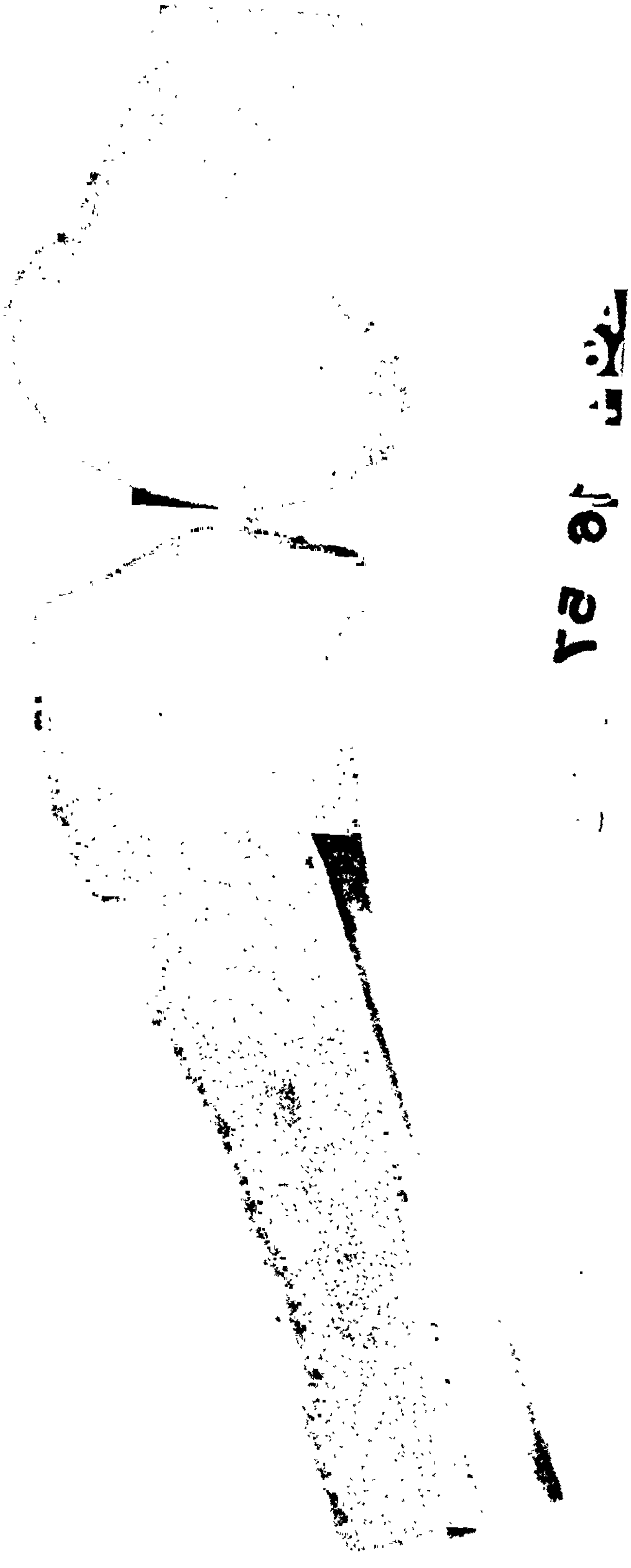

Fig. 5.—Roentgenogram of left femur, tibia, and fibula at autopsy: lateral view. Note marked sclerosis; defect in tibia is due to performance of biopsy three months previously.

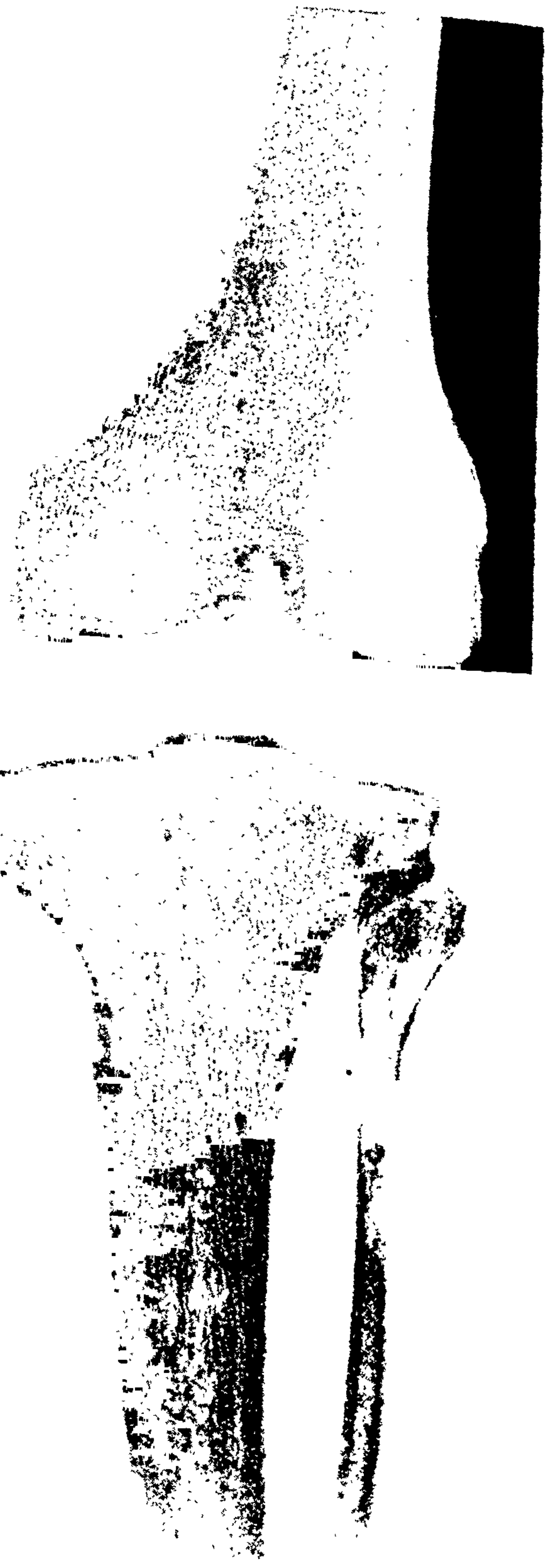

Fig. 6.—Anteroposterior view of bones shown in fig. 5.

X-ray therapy was given to the patient's tibia, the inguinal region, and the abdomen. Radiation sickness caused considerable weight loss. Despite all supportive therapy his general condition deteriorated rapidly, and the patient died about four months after admission.

Autopsy Findings.—The autopsy revealed generalized Hodgkin's disease involving the kidneys, spleen, liver, pancreas, thyroid, testes, prostate, and the left tibia. Sections taken through the tibia reaffirmed the diagnosis of osteitis deformans (fig. 4). At autopsy, the tissue between the bone trabeculae was almost totally necrotic, perhaps secondary to the radiation therapy (fig. 5 and 6).

Summary

A case of simultaneous occurrence of osteitis deformans (Paget's disease) and Hodgkin's disease in the same bone of a patient probably represents a fortuitous event. The concurrence of Paget's disease with other pathological entities has been reported. No relationship between the two fundamentally different disorders presented here was established.

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EOSINOPHILIC PNEUMONIA

REPORT OF TWO CASES WITH PULMONARY BIOPSY

Anthimos J. Christoforidis, M.D.
and
William Molnar, M.D., Columbus, Ohio

Two women, aged 49 and 39 years, had persistent fever, marked eosinophilia (33 to 39%), and roentgenographic evidence of ill-defined, shifting infiltrations in the lungs. Biopsy specimens were obtained in both instances. In the former case the most striking lesion was an infiltration of lobular septums and of the perivascular adventitia with eosinophils; in the other case the findings included a similar infiltration, which formed small masses of the type seen in lobar pneumonia. The first patient made a complete recovery after the biopsy. In the second patient the administration of 20 mg. of prednisone twice daily promptly abated the fever and caused the eosinophilia to disappear within one day's time.

The concept of eosinophilic pneumonia has changed considerably since it was originally reported by Loeffler[1] in 1932. He described it as a usually symptom-free condition, with incidental pulmonary findings of a few days' duration. The experience of others has shown that there is considerable variation in the severity of the manifestations as well as in the duration of this disease syndrome.[2] The symptoms may range from negative findings at physical examination to the clinical features of bronchopneumonia, and the duration can vary from a few days to several weeks or even months. Laboratory requirements for the diagnosis of the illness, however, remain the same; that is, a blood eosinophil count above 6% and the presence of pulmonary infiltrates.[2]

In the two cases of chronic pneumonia with eosinophilia reported here, a pulmonary biopsy was performed, although a preoperative diagnosis

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From the Department of Radiology and the Ohio Tuberculosis Hospital, Ohio State University Health Center.

of eosinophilic pneumonia was suggested, to clarify the nature of pulmonary infiltrates which lasted much longer than generally accepted for this disease syndrome.

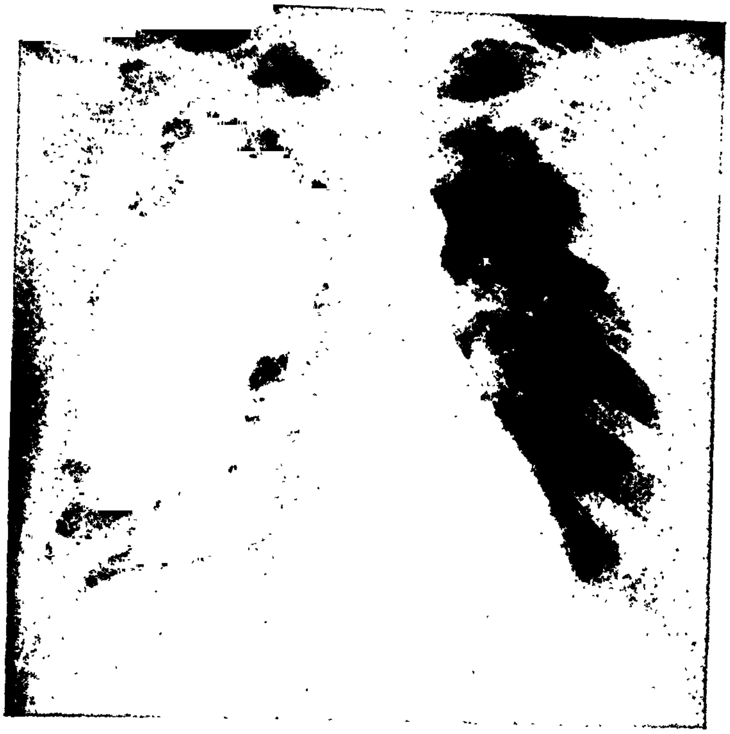

Fig. 1 (case 1).—Roentgenogram made June 8, 1955, showing *infiltration* involving lateral aspect of upper lung fields, mainly on left. Similar changes were also present in right lower lobe. *Hilar* lymph node enlargement is more prominent on left side.

Report of Cases

Case 1.—A 49-year-old woman was admitted to the Ohio Tuberculosis Hospital on June 17, 1955, with the chief complaint of general malaise and weight loss for the preceding six months. Past history revealed that she had been given a diagnosis of pulmonary tuberculosis in 1939 and treated for three years with bed rest on the basis of x-ray findings, although her sputum and gastric smears and cultures did not contain tubercle bacilli. There was no familial history of tuberculosis. In March, 1955, the patient stated that she had developed pneumonia which was treated with antibiotics; meanwhile, tubercle bacilli were allegedly found in one gastric smear. Her symptoms persisted and, in view of the "positive" gastric smear, the patient was referred to the Ohio Tuberculosis Hospital.

The physical examination on admission revealed a well-developed, well-nourished woman in no acute distress. Her temperature was 37.5 C (99.5 F), respirations 20 per minute, and blood pressure 118/70 mm. Hg. The chest was clear to percussion and auscultation.

Review of a chest film taken in 1951 showed no active pulmonary disease. A preadmission chest roentgenogram made on June 8 revealed confluent, ill-defined infiltration, involving the lateral aspect of the upper lung fields, mainly on the left, with similar changes in the right lung field adjacent to the costophrenic angle. There was evidence of bilateral hilar lymph node enlargement (fig. 1). Chest x-ray at the time of admission (June 18) showed extension of the infiltration along the peripheral aspect of both lung fields, including the left base. The hilar adenopathy became more prominent.

The patient was admitted to the medical service. Pertinent laboratory data on admission included white blood cell count, 10,550 per cubic millimeter, with 46% neutrophils, 20% lymphocytes, and 33% eosinophils. Fasting blood sugar level was 99 mg.%, and blood urea nitrogen level, 12.9 mg.%. Examination of the sputum showed about 90% eosinophils. Result of the tuberculin skin test was positive, and results of skin tests for histoplasmosis, blastomycosis, and coccidioidomycosis were negative. Although no definite diagnosis was established, the patient was started on chemotherapy with isoniazid (INH) and para-aminosalicylic acid (PAS) on the basis of the x-ray findings and one positive gastric smear which was reported from outside before the patient's admission to the hospital. Follow-up chest x-ray on Aug. 9 showed further extension of the infiltration in the left upper lung field while the consolidation became less apparent in both bases. A new infiltration appeared in the right middle lung field (fig. 2).

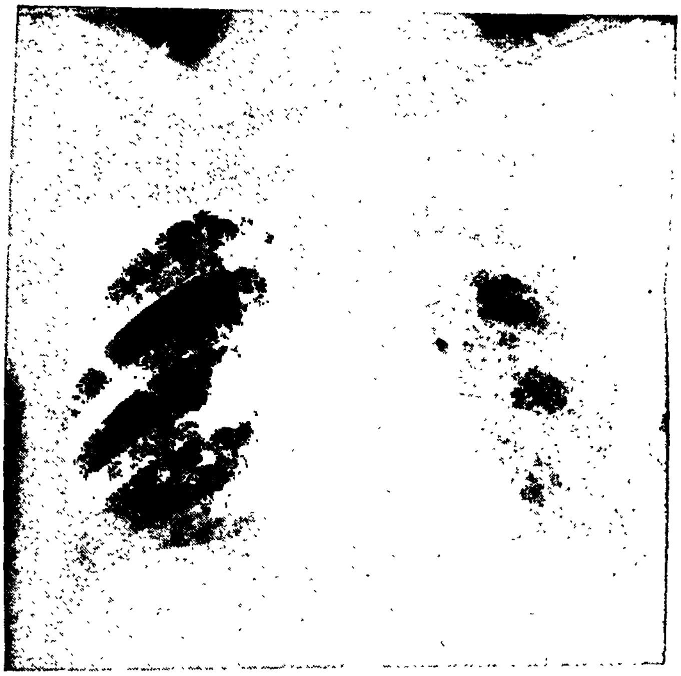

Fig. 2 (case 1).—Roentgenogram made Aug. 9, 1955, showing further extension of infiltration in left upper lung field and decrease of infiltration in both bases. New infiltration has taken place in right middle lung field.

The next examination, on Sept. 6, demonstrated a decrease of the ill-defined infiltration bilaterally. The patient's case was presented in the surgical conference and it was felt that lung biopsy would be of value in view of the fact that this infiltration had persisted for more than three months, in spite of drug therapy. All sputum and gastric smears and cultures for acid-fast bacilli were negative. Loeffler's pneumonia was suggested as a possible diagnosis, although it was felt that "the duration of the disease was longer than usually occurs in Loeffler's pneumonia and a biopsy was justified for more definitive diagnosis."

On Sept. 15 biopsy was performed on the left lower lobe. Microscopic examination showed the aveolar spaces to be generally empty, although an occasional space contained edema, fluid, or a clump of microphages. There was a generalized excess of lymphocytes which occasionally occurred in concentrated foci, suggesting lymph follicles. The striking lesion seen in the sections, however, consisted of an infiltration of lobular septums and perivascular adventitia with eosinophils. Usually adjacent to such sites in infiltration there were a few alveolar spaces consolidated by eosinophils together with microphages. The involved lobular septums or vascular adventitia were thickened by the infiltrations and showed a distinct excess of collagen. A few fibers of this collagen appeared excessively pink, but this so-called fibrinoid degeneration was inconspicuous. The media of the vessels failed to show evidence of inflammation or fibrinoid degeneration. Occasionally, one or perhaps a pair of alveolar spaces contained a nodule of young scar tissue, consisting mainly of fibrocytes with delicate collagen. It is clear that these represented organization of earlier foci of exudation. The pathological diagnosis was scarring and eosinophilic infiltration of the lung compatible with Loeffler's pneumonia.

The patient had an uneventful postoperative course and was discharged on Sept. 24, 1955. Follow-up chest x-rays on April 11, 1956, showed no evidence of infiltration in the lung fields.

Case 2.—A 39-year-old woman, with a history of bronchial asthma and chronic sinusitis for three years, had an insidious onset of weakness and malaise two to three months prior to admission. One month before admission, she began to have afternoon chills and fever up to 38 C (100.4 F). On Dec. 18, 1958, her first roentgenographic chest examination showed bilateral peripheral infiltration in the upper lobes, being more extensive on the right side (fig. 3). She received treatment with antibiotics from her family physician, with no apparent response. A repeat chest film made on Jan. 20, 1959, revealed further progress of the infiltration, which had become more extensive in the left middle lung field, with small areas of infiltration in both lower lung fields. Sputum studies and a tuberculin skin test gave negative results. In view of the persistent symptoms and progressive pulmonary infiltration, she was admitted on Jan. 29, 1959, to the University Hospital for further diagnostic studies.

There were no pertinent physical findings on admission. The chest was clear to percussion and auscultation. Her blood pressure was 110/70 mm. Hg, pulse rate 80 per minute, and temperature 37.1 C (98.8 F). Laboratory studies on the blood showed a hemoglobin level of 11.8 Gm.% and a white blood cell count of 6,750 per cubic millimeter, with 34% neutrophils, 23% lymphocytes, and 39% eosinophils. Results of a serologic test for syphilis and tests for typhoid fever, brucellosis, paratyphoids, histoplasmosis, blastomycosis, coccidioidomycosis, Q fever, and psittacosis were all negative. Marrow findings were normal except for an increased number of eosinophils. No parasites were found in the stool.

For the first three weeks of hospitalization, the patient had a spiking temperature up to 38.3 C (101 F). During the hospitalization, the eosinophil count varied from 40 to 11%; otherwise, the blood cell count showed no significant deviation from the initial values. Chest x-ray on Jan. 30 revealed regression of the ill-defined infiltration of the right upper lobe with persisting isolated consolidations in the rest of the lung fields, unchanged since the last examination on Jan. 20 (fig. 4). The patient's clinical condition during this period remained static. Although eosinophilic pneumonia was thought to be the most likely diagnosis, it was felt that this impression should be confirmed by a pulmonary biopsy, in view of the long duration of the progressive infiltrates, before any steroid therapy was administered. Microscopic sections of the specimen

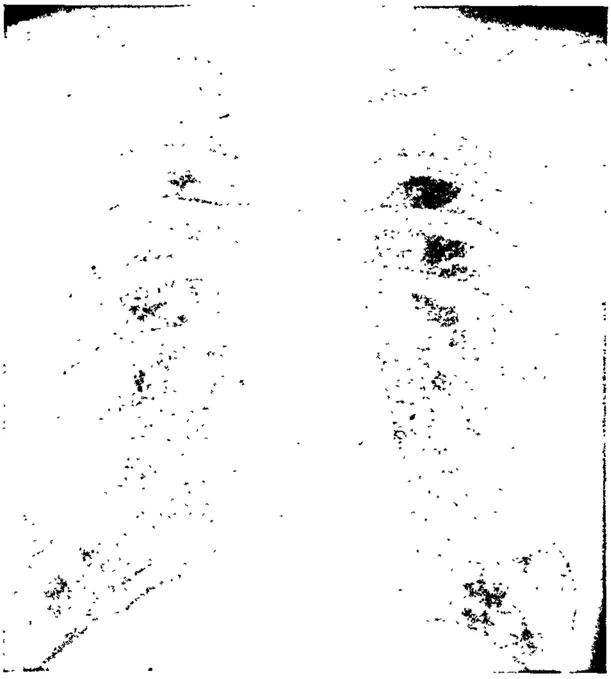

Fig. 3 (case 2).—Roentgenogram made Dec. 18, 1958, showing bilateral peripheral, ill-defined infiltration in upper lobes.

obtained from the pulmonary biopsy on Feb. 5, 1959, showed a nonsuppurative and nondestructive pneumonitis whose development and resolution was evident in the specimen. The sequential changes visible consisted of (1) proteinaceous edema within the alveoli, (2) a secondary infiltration of eosinophils with fibrin, forming small masses of the type seen in lobar pneumonia, and (3) a final infiltrate of the alveoli by macrophages. This later infiltration appeared to be the final stage in the development of the inflammatory process, and the macrophage cellular masses showed continued aggregation, with central necrosis which sometimes involved the contents of an entire alveolus. There was relatively little interstitial reaction, although a few areas of eosinophils could be seen within the interstices of the pulmonary tissue. This particular sequence of events is consistent with the type of clinical course associated with Loeffler's pneumonia (fig. 5). It was concluded that the findings were consistent with a diagnosis of Loeffler's pneumonia.

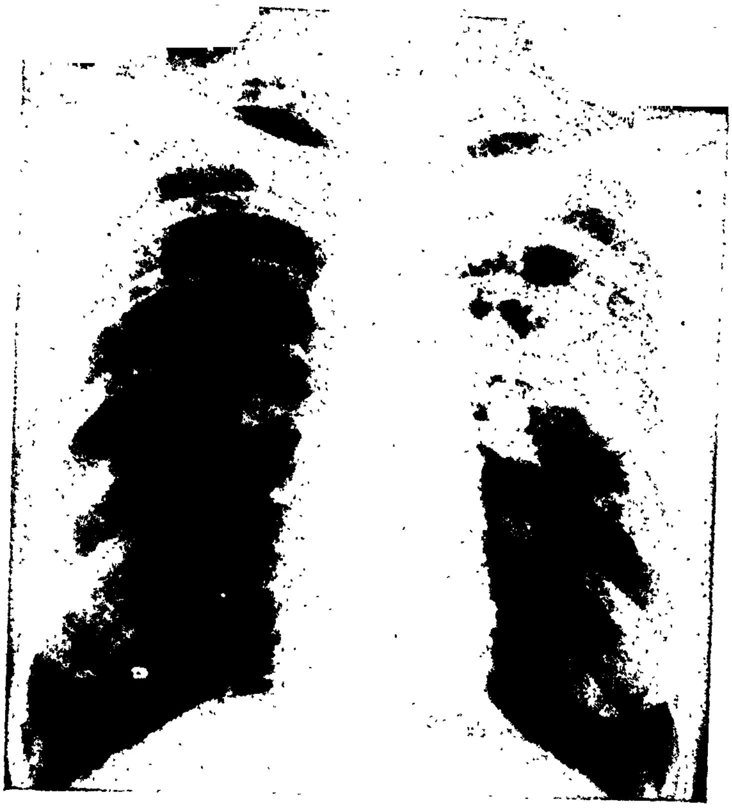

Fig. 4 (case 2).—Roentgenogram made Jan. 30, 1959, showing further extension of infiltration, especially in left middle lung field, with small areas of infiltration in lower lung fields.

On the basis of these findings, steroid therapy was introduced on Feb. 9 in the form of 20 mg. of prednisone twice daily. The patient responded promptly to the treatment. Her temperature returned to normal, the eosinophilia disappearing one day after the beginning of the steroid treatment. A chest roentgenogram made on Feb. 12 showed complete disappearance of the previously described infiltrations. A repeat chest roentgenogram made on Feb. 21 was essentially normal. She was discharged in good health 12 days after the pulmonary biopsy and was advised to continue taking 5 mg. of prednisone three times daily for one month.

Comment

The interesting feature in both cases is the relatively long duration of the pulmonary infiltrations associated with symptoms of fever, malaise, and elevated blood count with high eosinophil level. Eosinophilic pneumonia, used as a synonym for Loeffler's syndrome, was always thought to be a condition of relatively short duration, always benign, and manifesting pulmonary infiltration which disappeared within three to eight days.[3]

The usual benign character and short duration of the condition was offered as an explanation for the lack of tissue material for histological study, as predicted by Loeffler.[1]

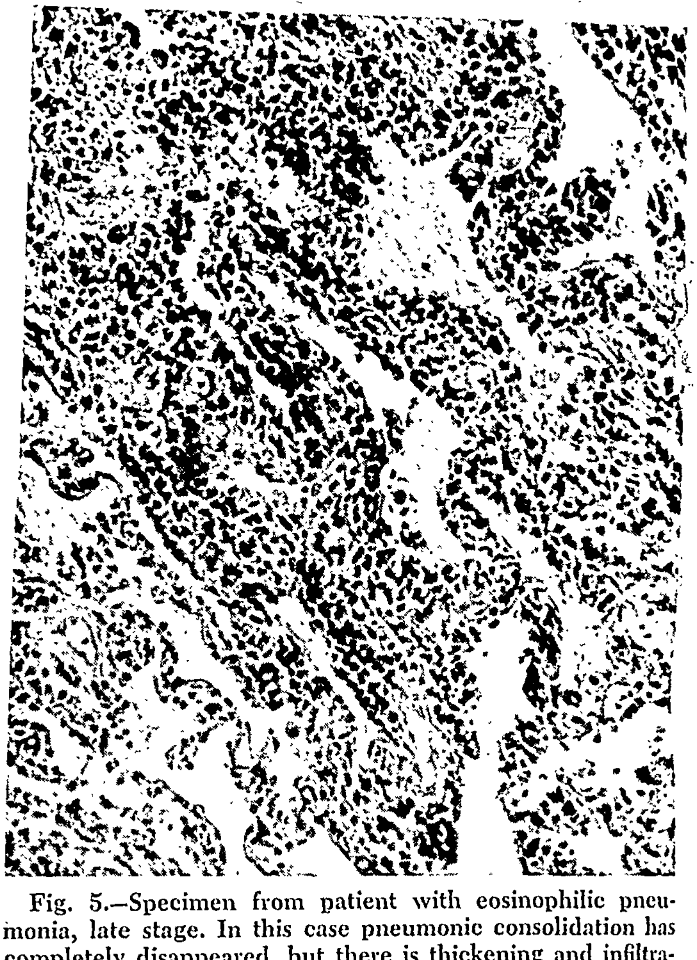

Fig. 5.—Specimen from patient with eosinophilic pneumonia, late stage. In this case pneumonic consolidation has completely disappeared, but there is thickening and infiltration of alveolar septums and perivascular areas by small cells with dense nuclei, eosinophils. Among eosinophils are scattered larger infiltrating macrophages or histiocytes. Resemblance between this appearance and that characteristic of eosinophilic granuloma is apparent (× 100).

The first description of microscopic examination was reported in 1942 and based on incidental autopsy findings.[1] The characteristic histological findings in the lungs were infiltrations by eosinophilic leukocytes and giant cells, associated with interstitial proliferations and serous exudate. There was no history of any clinical symptoms and unfortunately no roentgenograms were available. In 1945, Bailey reported histological findings of Loeffler's syndrome in an autopsied case, in which, in addition to a large number of eosinophilic leukocytes in the pneumonic exudate, there was advanced organization of the exudate with fibroblasts and giant cells. He called attention also to the presence of granulomatous lesions and necrotizing arteritis and phlebitis.[5] The only available roentgenogram of the chest was made more than four months prior to death, and no reliable correlation with the postmortem findings could be made.

Review of the literature up to 1958 shows that the only operative specimen was reported by Buckles and Lawless in 1950.[6] They performed a pneumonectomy on a patient with persistent pulmonary consolidation simulating a neoplastic lesion which had persisted for 14 months. The microscopic findings showed fibrosis and massive infiltration by eosinophils, periarteritis, and arteriolitis in addition to endothelial cell proliferation.

In the first of our cases the patient had abnormal radiologic findings of more than three months' duration and clinical manifestations of more than six months' duration prior to the pulmonary biopsy. In the second case the available radiologic findings lasted about two months, with clinical symptoms of four months' duration. The histological findings in the first case were of more advanced nature, with small foci of exudation showing organization and the presence of occasional nodules of young scar tissue. It is probable that in cases of long duration the pathological process can progress to an extent where fibrotic changes occur as well as vascular changes consisting of necrotizing arteritis and phlebitis. In such instances, in which there is no tendency toward spontaneous regression in a short time, usually one or two weeks, the administration of ACTH or cortisone, as a rule, results in dramatic improvement of the radiologic and clinical findings. with rapid return of the eosinophilic count to the normal level. This has been the experience of several authors.[7] In the second case the radiologic picture returned to normal in seven days after the administration of prednisone. The response to the steroid therapy also supports the theory of the allergic nature of this disease syndrome as it has been postulated by several authors and proved by Sprent,[8] who produced transient pulmonary infiltrations and eosinophilia experimentally by parenteral injections of ascaris extracts in previously sensitized animals. Similar findings were produced by parenteral injection of different allergens in animals which were previously sensitized against the specific antigen.[7b] Both of the cases presented here were in patients treated in the past for allergy manifested by chronic sinusitis and bronchial asthma.

The radiologic examination is the single most significant diagnostic procedure. The detection of migratory changes in the lungs, so important in the diagnosis, necessitates frequent x-ray examinations. The infiltrations are irregular, homogeneous, and of varying size and usually do not have lobar or segmental distribution. As a rule both lungs are involved, but the extent of the involvement can vary from patient to patient and also from one examination to another in the same patient. In these two cases the infiltrations had a tendency toward peripheral distribution. In the first case there was evidence of hilar lymph node enlargement (fig. 1 and 2). This is an unusual finding in view of the lack of lymph node involvement reported by others.[9]

The differential diagnosis of eosinophilic pneumonia should include pulmonary tuberculosis, especially when the infiltrations involve the upper lobes. It is probable that the first case was misdiagnosed in 1939; the patient was treated for pulmonary tuberculosis for two years without positive findings of acid-fast bacilli on sputum and gastric studies. The misdiagnosis of pulmonary tuberculosis in cases of eosinophilic pneumonia seems to be a relatively common occurrence.[10]

Peripheral eosinophilia was constantly present during the period of pulmonary manifestations. The degree of eosinophilia does not appear to be related to the extension of the pulmonary involvement. There was no pleural effusion in our cases, although this has been reported.[11]

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Dr. Philip C. Pratt, Department of Pathology, reviewed and made available the microscopic findings.

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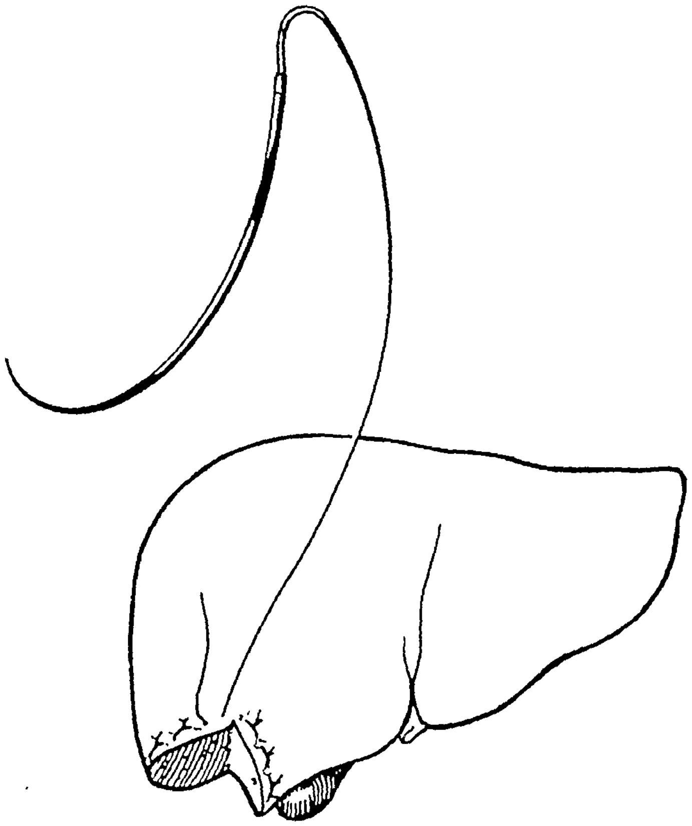
J.A.M.A., May 14, 1960

CLINICAL NOTES

NEW LIVER SUTURE

Richard D. Brasfield, M.D., New York

Current interest in hepatic resections[1] for various benign and malignant tumors has caused physicians at the Memorial Hospital to seek methods for decreasing blood loss. Bleeding from the point of suture has been most troublesome when the conventional eye-type needles and sutures are used. The doubled suture at the butt of the needle tears the thin liver capsule and vascular parenchyma, which results in massive blood loss during extended liver resections.



Use of atraumatic liver suture in wedge resection.

After four years of extensive clinical and laboratory trial at the Memorial Hospital with various sizes of sutures (000 to 3) and needles (1.0, 2.0, 3.0, and 3.5 in.) with blunt and taper points, our final choice was a size 1 chromic gut suture swaged on a half circle 3.5-in. taper point needle with a diameter of 0.046 in. This atraumatic suture permits an adequate amount of tissue to be encompassed in a single bite and is large enough to prevent cutting through the tissue when the ligature is tied without breaking (see figure). At the same time, it causes minimal bleeding because of its taper point and relatively small size at the butt of the needle. A similar 3-in. needle, swaged on size 0 chromic gut, has also proved useful. Individual smaller sutures may be used for the tiny vessels and bile ducts.

The sutures used in this study were Ohio Suture Product 322, sizes 1 and 0, and were produced by the Ohio Chemical Suture Laboratories, 1400 E. Washington Ave., Madison 10, Wis.

From the Memorial Hospital.

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PLAN OF THERAPY FOR TUBERCULOSIS.—A satisfactory scheme of therapy for all cases of active tuberculosis except those with the most severe lesions consists of the administration of isoniazid and p-aminosalicylic acid for one year. This combination of drugs is at least as effective as any streptomycin-containing regime and is more convenient, considerably less toxic, and more economical. The principal element in any treatment regimen for active tuberculosis in children is the presence of isoniazid. Administration of adequate amounts of this drug for one year will prevent the development of meningitis. The daily dosage of isoniazid that we currently employ is 10 mg./Kg./day, given in two doses every 12 hours. This is supplemented with 0.2 Gm. of p-aminosalicylic acid/Kg./day divided into four doses every six hours. The availability of adequate drug therapy for tuberculosis should not cause neglect of other important aspects of management.—E. M. Sewell, M.D., The Initial Management of Primary Tuberculosis, *Quarterly Review of Pediatrics,* October-December, 1959.

TRANSIENT NODAL RHYTHM AFTER CONTACT WITH ALTERNATING CURRENT

William B. Bryer, M.D., Seattle

A-V rhythm has been produced experimentally in mammalian hearts by damaging (pinching or destroying) the sinus node. Produced in this way, the A-V rhythm is a substitute rhythm or passive heterotopy. A-V rhythm as active heterotopy has been successfully produced by stimulating the left accelerator nerve or by warming the A-V node.

It was proved that strong reflex stimulation of the vagus may suppress the S-A activity and may cause nodal rhythm.

The electrocardiogram of A-V rhythm usually consists of a normal electroventriculogram and of an electroauriculogram characterized by a negative P wave preceding the QRS complex by an abnormally short interval or succeeding it, or by the P wave's being buried in the QRS complex. If the stimulus starts from the upper part of the node, the atrial contraction slightly precedes the ventricular. If, on the other hand, the stimulus starts from the lower part of the node, the ventricles contract first.[1]

Etiology of A-V (Nodal) Rhythm

Nodal rhythm may occur (1) whenever the sinus node is depressed due to organic heart disease or vagal stimulation; (2) during infectious disease (e. g., rheumatic fever, scarlet fever, and typhoid); (3) during treatment with digitalis or strophanthin—the action of these drugs being considered as delaying conduction in the A-V system directly, or indirectly by increasing vagal tone, or, after the use of quinidine sulfate or procainamide (Pronestyl) hydrochloride for the interruption of a paroxysmal ectopic tachycardia; (4) after myocardial infarction; (5) when carotid sinus pressure causes nodal rhythm through vagal stimulation; (6) during cardiac catheterization or cardiac surgery; (7) as a consequence of electrolyte imbalance; and (8) when any organic damage occurs to the sinus node.[1A]

Electropathology

Tension (Voltage).—Both low-voltage and high-voltage currents can cause fatal accidents.

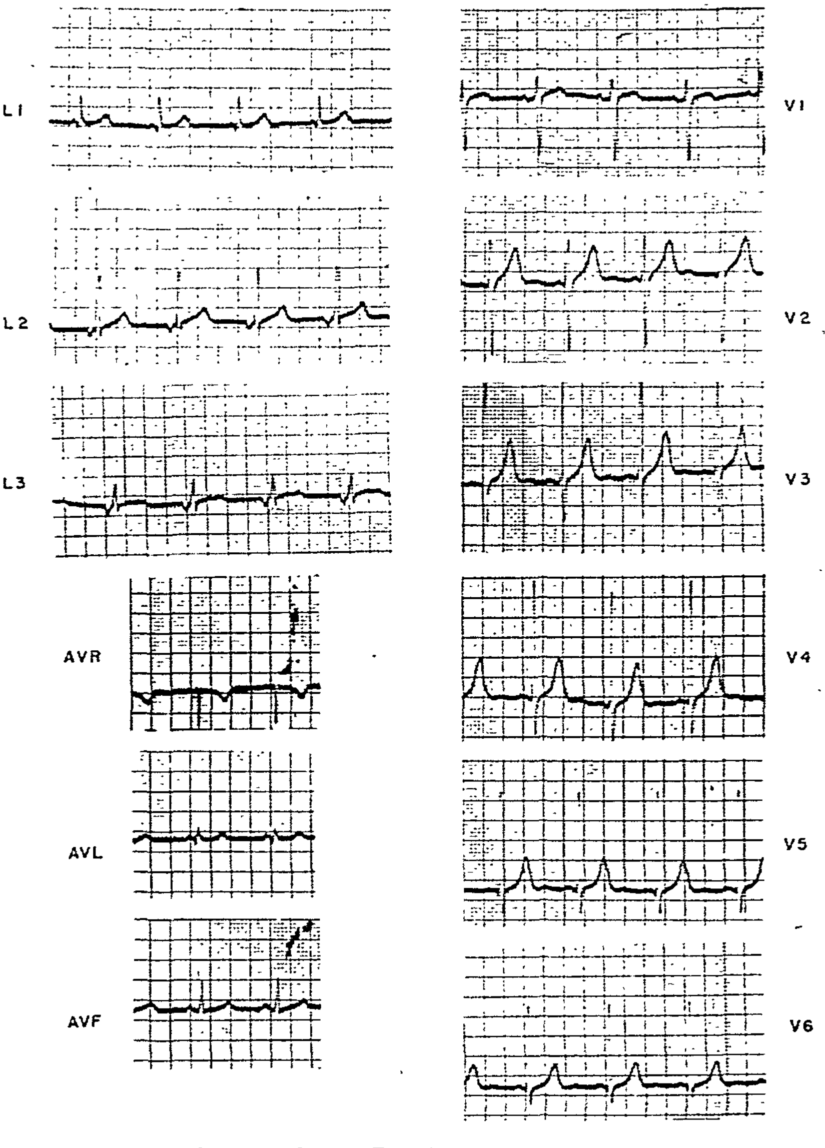

Fig. 1.—Electrocardiogram taken on Dec. 20, 1955, showing typical nodal rhythm: P_1 normal, P_2-P_3 inverted and deformed, and P-R shortened to less than 0.1 second.

Low-Tension Currents: Even a current as low as 60 volts has been proved to be fatal, especially when the current has passed through the heart. The most common cause of electric shock due to currents of low voltage is electric lamps: When a per-

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son is well grounded (such as being in a bathtub or wearing shoes with metal taps) and touches a charged part of an electric lamp with his hand—especially the left one—he may be killed instantaneously by an electric current of only 110 volts.

High-Tension Currents (Between 1,000 and 200,000 volts): Accidents with high-tension currents usually occur in electric plants, when persons are either standing on iron steps or clinging to a metal railing around the generator.

Intensity (Amperage).—The intensity of an electric current in a given conductor is its tension divided by the resistance of the conductor, which, in the case of electric shock, is the human body. This resistance offered by the body to the flow of current consists of two parts, namely (1) that offered by the skin at the points of contact and (2) that offered by the tissues.

Dry skin is an excellent insulator, but when it becomes moistened it loses its insulating properties. The resistance of the tissues, once the current gets inside the body, is practically a pure resistance. In accidents to human beings the intensity (amperage) cannot be determined exactly, because, for the reasons mentioned above, the resistance of the body at the moment of the accident is unknown and cannot be reconstructed.

Type of Current.—Direct currents are definitely less dangerous than alternating currents. The number of cycles per second (cps) of an alternating current is of great importance. Alternations between 40 and 150 cps are most dangerous. These are the alternations most commonly found in industrial currents. Higher numbers of cycles are less dangerous. Human nerves and muscles are not at all sensitive to frequencies as high as 500,000 to 1,000,000 cps. Therefore, these types of frequencies are used in physiotherapy machines—20,000 to 40,000 volts, from 1 to 2 amp., and about 1,000,000 cps.[2]

The Heart and the Electric Current

Autopsy.—Postmortem examinations of electrocuted persons do not reveal much detailed information. Gubler[3] found loosening and ruptures of the myocardial fibers and fibrils. In addition to the above findings, Kawamura reported some minute hemorrhages in the myocardium.[4] Clinically, electric shock may cause to the heart (1) premature beats; (2) auricular flutter; (3) auricular fibrillation; (4) paroxysmal tachycardia; or (5) ventricular fibrillation. Any of these changes are usually transient except ventricular fibrillation, which may cause death.

Report of a Case

On Dec. 20, 1955, at 2:30 p. m., a 46-year-old male electrician, while engaged in his work, came in contact with an electric current of 220 volts and 115 amp. with both hands. The patient, who was sitting on the floor, was hurled backward the length of the room—a distance of about 12 ft. He did not lose consciousness, and he felt a burning sensation in both hands. At about 5 p. m., he complained of precordial pain which worried him. A physical examination made at about 9 p. m. did not reveal anything abnormal. His pulse was regular and firm at 80 per minute. Blood pressure was 160/88 mm. Hg. The heart size and configuration were normal. No murmurs were heard. Both palms showed 1st-degree burns. An electrocardiogram showed typical nodal rhythm: P_1 normal, P_2-P_3 inverted and deformed, and the P-R interval shortened to less than 0.1 second (fig. 1). Atropine, 1/100 grains (0.60 mg.) every four hours, and rest were prescribed.

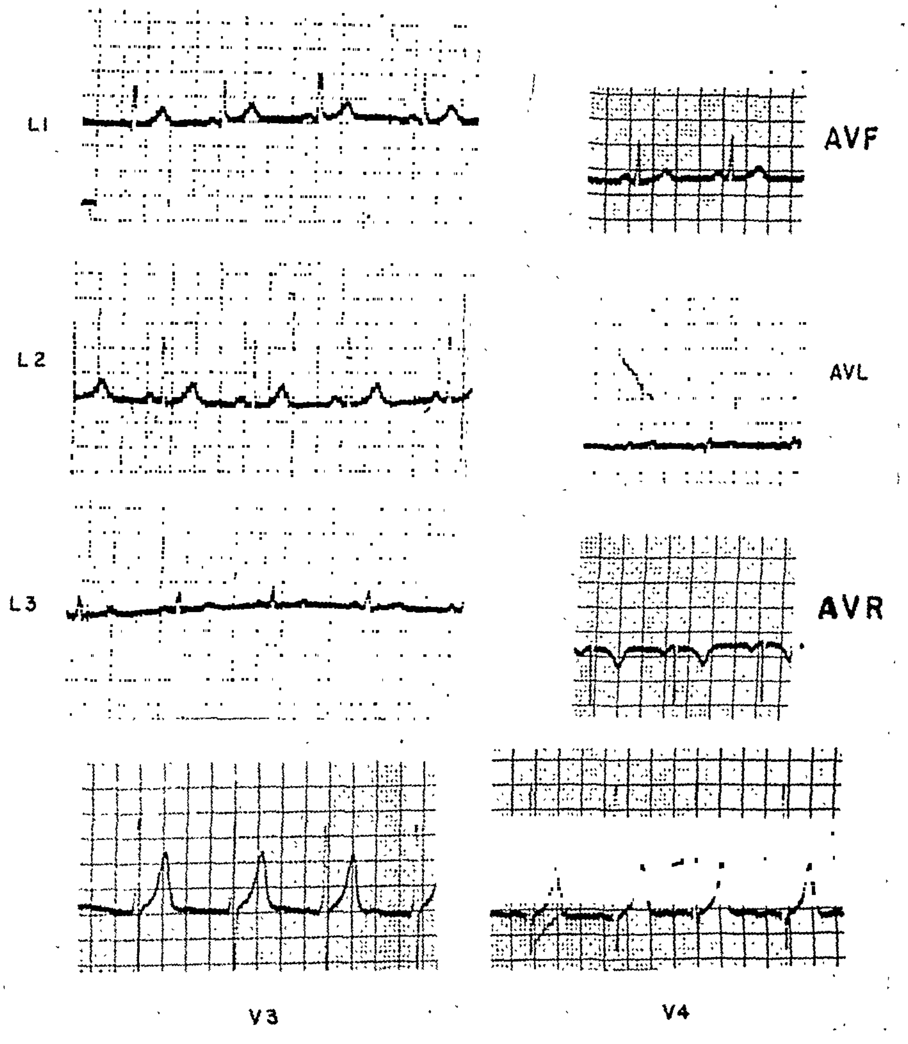

Fig. 2.—Electrocardiogram taken on Dec. 24, 1955, showing normal sinus rhythm.

On Dec. 23, at 7 p. m., the patient's left arm and left leg suddenly felt weak and numb; he could move them only with difficulty. The left side of his face also felt weak and numb. On examination I found a left-sided hemiparesis, with the central facial type of paresis since the frontalis muscle was entirely spared and showed complete function. His speech was undisturbed. Furthermore, left-sided hemihypesthesia to touch, heat, and cold was found, and the muscular sense and vibratory sensation were also diminished.

Nodal (A-V) Rhythm in Person Exposed to Electric Current of 220 Volts and 115 Amp.

Date, Dec., 1955	Clinical Status	Rhythm	P Wave	P-R Interval, in Lead II, Sec.	Blood Pressure, Mm. Hg
20	Day of electrical Injury	Nodal	Inverted	0.09	160/88
23	Hemiparesis				150/80
24	Hemiparesis	Sinus	Normal	0.14	156/84
25	Recovered				
30	Recovered	Sinus	Normal	0.14	160/80

On the next day (Dec. 24) the ECG showed normal sinus rhythm (fig. 2). On Dec. 25, all the paretic signs and symptoms disappeared (after 48 hours' duration).

Comment

As was previously mentioned, several causes of nodal rhythm—such as drugs, infections, and myocardial infarction—have been described in the medical literature, but contact with electric current has never been mentioned as a precipitating factor. Therefore, it seemed fitting to present this case. The mechanism could be twofold: (1) by direct peripheral action of the current on the heart and (2) by central stimulation of the vagus nerve, especially of the centers of the vagus nerve in the medulla oblongata.

It is thought that the establishment of the nodal rhythm in the case described was due to direct action of the electric current on the heart itself, because the nodal rhythm appeared either immediately or at least within hours, considering that the ECG made on the same day showed nodal rhythm. The hemiparesis as a sign of brain damage commenced three days later. Therefore, the central action of the electric current on the vagus centers in the medulla oblongata was considered to be improbable. The brain damage causing the transient hemiparesis and hemihypesthesia probably was due to edema or minute hemorrhages in the brain. These are the most common lesions of the central nervous system caused by damage from electric current that have been described by pathologists. Other lesions which cause permanent damage have been described. In fatal cases, autopsies have revealed the following pathological changes: destruction of the Nissl's bodies, chromatolysis of the ganglion cells, rupture of the nerve cells, dislocation of the nucleoli, loosening of the glia, vacuolation of the nerve cells, and close position of the nuclei to the wall of the cells; breaking up of the tigroid in the medulla oblongata into small granules; and the complete destruction of the nerve cells, with extrusion of the nuclei.

Summary

Transient nodal rhythm, probably due to direct action on the heart itself, can occur after contact with alternating current. Since a review of the available world literature fails to reveal alternating current as a participating factor, it was considered relevant to report this unusual case.

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CATERPILLARS AS POISONOUS ARTHROPODS.—Although the caterpillar has been studied for some time, the exact nature of its irritant principle is still not known definitely. Its polypeptide nature is suspected. . . . The poison glands of the caterpillar appear similar to the salivary glands of the other arthropods of dermatologic interest. The skin reactions vary according to the sensitivity of the individual. The universally irritant caterpillars, although uncommon, appear to offer interest as a laboratory tool for the dermatologist studying enzymes concerned in the itch phenomenon. With extensive areas of poison glands available, caterpillars may supply good sources of material for itching. . . . Because of the irritant nature of caterpillars attempts should be made in work, farm, and field, and even in the home to avoid skin contact and especially eye contact. Systemic reaction of a severe type may occur.—L. Goldman, M.D., F. Sawyer, A. Levine, J. Goldman, S. Goldman, and J. Spinanger, B.S., Investigative Studies of Skin Irritations from Caterpillars, *Journal of Investigative Dermatology*, January, 1960.

COUNCIL ON FOODS AND NUTRITION

Report to the Council

The Council has authorized publication of the following report.

Philip L. White, Sc.D., *Secretary.*

AWARD OF RESEARCH FELLOWSHIPS IN CLINICAL NUTRITION

Ten fellowships for research in clinical nutrition have been awarded by the Nutrition Foundation, Inc., and the Council on Foods and Nutrition. They have been given in honor of Dr. Carl V. Moore, recipient of the 1959 *Joseph Goldberger award in clinical nutrition.* A fellowship is granted to a medical student to permit him to carry on research in some phase of clinical nutrition during the nonacademic portion of the school year. Each grant consists of $600. Application is made by a senior investigator, and the fellowship is administered by him. The Council was impressed with the interest shown in these fellowships and had a difficult time selecting 10 from the many meritorious applicants.

This fellowship program is a part of the joint effort of the Nutrition Foundation, Inc., and the Council on Foods and Nutrition to stimulate staff members and students of schools of medicine to take a more active interest in the science of nutrition as an integral part of medical practice.

The 1960 fellowships have been awarded for the following research:

1. Nutritional status of Negro children with sickle cell anemia. Senior investigator, Roland B. Scott, M.D., department of pediatrics, Howard University.
2. Effect of diet on activity of alpha-glycerophosphatase in the rat. Senior investigator, David L. Drabkin, M.D.; student, Ernest Rosato, department of biochemistry, University of Pennsylvania.
3. Fat absorption by isolated small intestine in vitro. Senior investigator, Arthur B. French, M.D.; student, William Swartz, department of internal medicine, University of Michigan.
4. Fat absorption in patients with severe intestinal parasitosis. Senior investigator, Milton E. Rubini, M.D.; student, Pedro Mayol, department of internal medicine, University of Puerto Rico.
5. Vitamin B-6 in transamination. Senior investigator, Alton Meister, M.D., department of biochemistry, Tufts University.
6. Metabolism of histidine (role of non-CoA derivatives). Senior investigator, Robert C. Baldridge; student, Ramon Burket, department of physiological chemistry, Temple University School of Medicine.
7. Effects of protein malnutrition on schistosomiasis. Senior investigator, Seymour Garson, Ph.D.; student, Manual C. Morales, division of physiological parasitology, University of Puerto Rico.
8. Relation of blood enzymes to nutritional status. Senior investigator, Myron Brin, Ph.D.; student, Jerry Schwartzburg, department of biochemistry and medicine, State University of New York.
9. Secretion of alcohol into the stomach from intravenously administered alcohol. Senior investigator, Basil I. Hirschowitz, M.D.; student, Don W. Powell, department of medicine, division of gastroenterology, University of Alabama.
10. Study of enzyme hydrolysis of anserine to B-alanine and 1-methyl-histidine. Senior investigator, L. C. Smith, Ph.D.; student, Duane T. Freier, department of biochemistry, State University of South Dakota.

A FUNDAMENTAL ATTACK ON MENTAL DISEASE.—Monoamine oxidase destroys serotonin in the brain and other tissues. If, therefore, monoamine oxidase is inhibited, higher concentrations of serotonin will be able to act for long periods in the brain, the heart, the bronchi and other organs. If, as has been postulated, the serotonin deficiency is associated with mental disease, the monoamine oxidase inhibitors may be useful in some forms of mental disturbance. Among other conditions in which these monoamine oxidase inhibitors may have some effect are drug and alcohol addiction, peptic ulcers, disorders of the clotting mechanism and deficiency in muscle tone.—M. Fishbein, M.D., Monoamine Oxidase Inhibitors and Vascular Disease, *Angiology*, February, 1960.

SPECIAL CONTRIBUTION

The following paper was read by Leo W. Simmons, Ph.D., Professor of Education (Sociology), Teachers College, Columbia University, at the opening plenary session of the ad hoc Advisory Committee to the Committee on Scientific Activities of the Board of Trustees of the American Medical Association, at Hershey, Pa., Sept. 14, 1959.

IMPORTANT SOCIOLOGICAL ISSUES AND IMPLICATIONS OF SCIENTIFIC ACTIVITIES IN MEDICINE

Leo W. Simmons, Ph.D., New York

I wish to propose four assumptions to be used as a "platform" for further discussion of the problems selected for our conference deliberations. It is for those more closely affiliated with the medical profession to consider whether these assumptions have validity in the present state of medical developments.

Sociological Assumptions Concerning Modern Medicine

First, modern scientific medicine, with its storehouse of knowledge and skills, is already able to make new and outstanding contributions to the contemporary problems of both physical and mental health. Amazing therapeutic potentialities appear to be available or in the offing.

Second, modern scientific medicine confronts a substantial resistance to the full and forthright practice of its therapeutic potential. Resistance ranges from apathy to opposition—partly overt, partly hidden, sometimes conscious and sometimes unconscious on the part of recipients of some medical service. The medical practitioner is rarely permitted by society to utilize his knowledge and skills maximally. The obstacles to the application of medical care can be almost as great as are those to the discovery of effective therapies. In short, the task set for health care is only half accomplished by discovery of new medical skills; the practitioner can still encounter sick and dying people around him and, despite his knowledge of what to do, be helpless to do it. This statement is made as an assumption. Is it also a fact?

Third, there follows what may be regarded as a philosophical or a moral assumption in relation to the medical professional code. This code contains an implied responsibility of or a challenge to the physician to fulfill his therapeutic function for the people whom he elects to serve in spite of their apathy or opposition, or at least to do so to some substantial degree in the face of these difficulties. A cardinal criterion of good professional conduct is that the physician should know better than do his clients what service they need and that he be committed to work positively toward such ends. This involves an obligation to operate on a superior level than that which is customarily associated with such terms as salesmanship or propaganda. A truly professional worker endeavors, even against opposition, to provide for his clients what he recognizes to be their needs from his specialty, even though they cannot possibly understand the necessity for such services.

Fourth, there exists a potential knowledge or know-how in the "application" of medicine that is subject to systematic study. Such knowledge, which can be acquired from medical successes as well as from failures, can gain acceptance for the services to be rendered. This field of study is especially relevant to the interests and skills of the behavioral or social sciences.

Emerging Goals in Modern Medicine

The second topic with which I am concerned is the emerging goals in modern medicine. It behooves me as an interested layman and potential patient to raise some questions for clarification.

As I understand it, the primary purpose of the professions in the field of health is to control disease and promote health. This goal is voiced by the leading figures and professional organizations in the various medical, nursing, and other health specialties. The central aim, as frequently expressed, is the continuous improvement of medical care or patient welfare. It is difficult, however, to define either health or patient welfare. Definitions of both are frequently given more in negative than in positive terms. Health, for example, often is defined as the absence of disease or disability and patient welfare as relief from suffering or discomfort. There appear to be trends, however, toward more positive definitions. The World Health Organization provides one notable example: Health is "a state of complete physical, mental, and social well-being and not merely an absence of disease or infirmity."

From Teachers College, Columbia University.

A positive definition of health can also be made in a more down-to-earth manner. According to Dr. Roger I. Lee and Lewis W. Jones in "Readings in Medical Care" (edited by the Committee on Medical Care Teaching of the Association of Teachers of Preventive Medicine, 1958), the objectives of good medical care are defined in positive and specific terms. In more specifically defining the issues they make the points that good medical care (1) limits itself to rational medicine based on the medical sciences, (2) emphasizes prevention, (3) requires intelligent cooperation between the lay public and the practitioners, (4) treats the individual patient as a whole, (5) maintains a close and continuous personal relation between physician and patient, (6) makes use of and collaborates with social welfare workers, (7) coordinates all types of medical services, and (8) implies application of all the necessary services of modern scientific medicine to the needs of all the people.

If this is the promise of medicine for the future, then it is not difficult for a patient to recognize a great lag between the medical care he appears to be receiving and these great objectives. It is a splendid goal, which calls for positive and improved personal and organizational relationships on all levels and in all fields of medicine.

What the future system of institutional medical care in the United States will be is hard to predict. As far back as 1926, changes of great import appeared evident to some persons in positions of leadership. This is illustrated by the remarks of George E. Vincent, then president of the Rockefeller Foundation: "It looks as if society means to insist upon a more effective organization of medical service for all groups of people, upon distribution of costs of services over large numbers of families and individuals, and upon making prevention of disease a controlling purpose. Just how these ends will be gained only a very wise or a very foolish man would venture to predict. One thing seems fairly certain: in the end society will have its way."

In 1950, Willard C. Rappelye, then dean of the Faculty of Medicine and vice-president in charge of medical affairs at Columbia University, wrote: "Medical security in this country is coming and it is up to our profession to formulate ways and means by which sound, progressive plans can be drafted. It would be short-sighted and, in the long run, futile to ignore the broad implications of medicine, which must be recognized as much a social as a biological science." He stated further that, "Anyone who today disregards the relationship of medicine to current social, economic, and political conditions must be literally unwilling to face the facts." This statement was made a decade ago; its truth is even more obvious today.

The keynote of these forecasts, which now approach reality, is the necessity for and expediency of intelligent adaptation by the medical profession to the changes that are occurring in the social order and that seriously affect the future of medical practice.

Changes in the Social Order

What are the changes in the social order that so critically affect interpersonal and interprofessional relationships in medical practice? Some are very broad changes that are shaking the old foundations. There are others within the medical institutions themselves that are upsetting the old order of staff-patient relations. These two sets of forces can be divided into the broad outside and the more specific inside changes in the social environment.

Broad Outside Changes.—Of the broad changes that are in progress in the social order, six are of particular relevance to modern medicine.

First, there is the increasing mobility of the population. We Americans are moving over the earth at a rate and pace previously unknown to man and are shifting our homesites repeatedly in the course of a lifetime. Such constant movement complicates the issue of continuity in medical care and the interpersonal relationships involved.

To this horizontal movement must be added our status seeking or social mobility, through which we hope to move up the status ladder at least one rung per generation. Shifts in social status are followed by shifts in standards and norms of consumption; consequently, Americans want not only better homes and better clothes but also better medical care. We have thus become doubly nomadic, both on a horizontal and a vertical plane. Such population mobility is bound to upset established norms and expectations in medical practice.

In the second place, today's American public of potential patients is becoming increasingly sophisticated. There was a time when physicians knew more about almost any topic than did almost anyone with whom they came in contact. Medical personnel used to enjoy the status of an intellectual aristocracy. This is no longer true. Today, almost every physician, even one who practices in a semicivilized spot in America, faces patients who know, or think they know, more about many matters than their physician can possibly know.

One physician, a general practitioner, recently was heard to say that it was "disturbing" what some of his patients knew, "even about medical matters." He added that his patients attempt to diagnose their own illnesses, bypass him, and go directly to a specialist. Later in the discussion a specialist commented that some of his patients even prescribe their treatment—"Doctor, a little penicillin, please." Such instances are extreme, to be sure, but the fact remains that contemporary Americans, when compared to their grandparents, are increasingly sophisticated and critical about the medical services they receive.

A third broad change affecting medical service is what has been called the "commercialization of the professions." At one time, the services of people in the professions seemed, in a sense, "beyond price." Some physicians, clergymen, and professors pursued their careers almost without regard to material gain and "stayed at their stands" when offered several times their earnings to practice their professions elsewhere.

A great change has been taking place in the professions. The formerly dedicated professional men have become substantially commercialized. Today a professor is thought of less as an academic "long hair" and more as a "sharp" businessman, and physicians are seen without their traditional halos, as fairly typical human beings with skills to sell—at a price. Recently two disturbing books were published: "The Academic Market Place," which describes how young professors get their positions and promotions, and "The Doctor's Business," which follows the same market-place approach. Who or what can stem the tide of commercialism that is sweeping over us?

A fourth change of major significance is the shift in age composition and prevalence of disease in the American population. Thanks to effective preventive measures, the communicable diseases have been largely eliminated. On the other hand, the increase in age of the American population has centered attention in medical and hospital practice on the chronic, long-term illnesses. When dealing with the communicable diseases, medical personnel did things mostly to or for patients. In treatment of the chronic diseases they have to depend more on the patient's cooperation in the therapeutic programs. This in itself calls for many modifications in the old norms of staff-patient relations.

In the fifth place, there is a transition in American thought from a religious-philosophical orientation toward a materialistic and scientific attitude to life and its problems. We are oversold on the idea that science can do almost anything for us—and then find ourselves distraught by the fact of its limitations. Outside its legitimate bounds, the scientific approach provides little help and cold comfort.

Finally, a sixth broad outside change has been the growth and spread of organized interest groups. Americans have become a highly organized people, with such groups as organized labor, organized professionals, organized producers, and organized consumers as well as organized salesmen. It appears as though we must organize or perish. The union card of an organized group with its bargaining and pressure apparatus seems all but a necessity today for obtaining whatever we consider to be our rights, our dues, or our needs. This development has entered also the health field and is altering old norms and patterns in medical care. Witness, for example, governments, unions, and other organized interests that are engaged in bargaining for medical services or are building their own hospitals, hiring their own medical personnel, and shaping their own system of medical care.

Changes Within Medical Institutions.—The broad outside changes in the American social order are accompanied by at least five significant changes inside the institutions and practices of medicine which affect the relations between patients and personnel.

First, there is the vast expansion of medical equipment or armamentarium, as it is sometimes called. Compared to the "little black bag" that was their stock-in-trade for diagnosis and treatment in the yesteryears, the equipment that doctors may command today has increased vastly in numbers and complexity. In capital outlay for plant and equipment alone, medical practice has become a giant enterprise—a far cry from the horse-and-buggy projects. Needless to say, the skills, functions, and relationships of the professional workers in the field of health have had to keep pace with the expansion of equipment and techniques. Medical personnel have become attendants to gadgets and documents as much as or more than to patients directly, and, in the eyes of the patient, doctors and nurses resort more and more to forms of remote control in their ministrations.

A second change consists in the elaboration of institutionalized medical care. To a significant degree, doctors, the nurses, other medical personnel, and patients have become cog units in an ever more tightly structured system. Thus their behavior (including perhaps, the way they think and feel) becomes, like the links in a chain, patterned and interlocked into procedure-processes somewhat similar to the "production line" in industry. As a result, the freedom of the physician is restricted and the ingenuity and spontaneity of the nurse limited, while the patients feel that their uniquely personal characteristics are slurred over, neglected, or squelched.

It is now common to speak of the "structure and culture" of a hospital as a phenomenon which, in important respects, is distinct and different from the social structure and culture of the community that surrounds it. It is part of the task of social scientists to study the institutionalized medical system as such to discover when and where interpersonal conflicts and stresses between medical personnel and patients are primarily the consequence of the system rather than of individual idiosyncracies.

A third change in medical institutions has been the rapid increase of medical and paramedical specialties and their application in varied types of services rendered to patients. This requires the adaptation of medical care to the fact that the patient, surrounded by an increasing host of specialists and in his role as a model patient, is expected to adapt, chameleon-like, to each in turn. To add to the patient's confusion, these varied "specialists" are, not infrequently, very sharply dividing up areas of their responsibility, contending or competing for positions, prerogatives, or for pay in correspondence with their conceptions of their particular competences.

If the patient can gain sufficient composure to observe carefully what is going on around him, he will recognize two kinds of specialists. They are (1) the scientific specialists who have learned more and more about less and less in the field of disease and patient problems, the experts who are, of course, indispensable and expensive, and (2) the "factory-trained" specialists who, to do it passably well and cheaply, have been quickly taught a little about a small task. They used to be called attendants and were dispensable and replaceable but are now moving up the prestige ladder, with more dignified titles and labels and increased prerogatives and pay.

The limitations and complications of spawning specialization and fragmentation of services around the patient are products of our times and constitute as yet unsolved issues in interpersonnel relations in the field of health care. As a natural component of specialization, interdependency of personnel results in a sharp splitting up of individual responsibility and of pinning down the blame on those who fail in the linked segments of responsibility. It has always been puzzling how quickly, and perhaps unerringly, the finger of blame points in a hospital. One might wonder if evil motives were attributed more readily in hospitals than elsewhere or if the personnel mistrusted each other more than is usual in other environments. Then it might dawn on one that the practice of blaming personnel is a built-in part of the system, with checks and counter-checks and maintained largely by the system. It may help to insure discipline, but the customary pattern does not help much in shedding light on the understanding of individual behavior. The apportionment of blame in the hospital deserves considerable systematic study.

A fourth important change within medical practice has been the broadening perspective on medical care, or what is considered to constitute good patient care. The old perspective was focused on the treatment of acute illness and, as a matter of fact, the modern hospital arose to provide treatment for such emergency ailments, for the mentally ill and for indigent persons. Today's conception of patient care has greatly extended its horizons.

The concept of patient care has been expanded to include preventive measures on the one hand and rehabilitative provisions on the other. More than that, this new concept leaves room for comprehensive patient care, which includes all the services that the varied specialists can contribute to the well-being of the patient. This expansion in our ideas of improved patient care overrides the traditional views. To try to fit these contemporary concepts into the old pattern of patient care resembles, figuratively, the attempt to fill old wineskins with new wine.

A fifth, and the last, significant change within the confines of medical institutions and practices that needs to be listed has been the rapid growth of prepayment plans, the rise of group medical practice, and the greater involvement of the government in medical provisions. These three more or less simultaneous developments carry in themselves the potential for profound modifications in professional-patient relations.

Let us consider prepayment plans for medical care. Heretofore, on entering a hospital as a patient under the old system of payment, most of us have been subjected to the full authority of the staff. When an issue arose and became sharply drawn between the patient and the hospital authorities of various ranks it did, not infrequently, boil down to this: the hospital or medical authority would say to the patient, "If you don't like it here, you can go elsewhere." If the patient did so, "discharged against advice" might then be written into the record. This practice is in order if the patient is a "charity case," or if he is a private patient paying his way on the spot; but it carries a sour, unfair, and nearly intolerable connotation when the patient has been paying for this service for 10, 15, or 20 years and has now come to get his prepaid medical care. It is entirely out of order to make a proposition to "take it or leave it" to the medically insured patient. He has a stake in the firm. Moreover, the cost of medical service has become so magnified that to pay once is all that most persons can muster. Today's patient cannot go elsewhere on a whim. Indeed, the price of available patient care has become so great that it is now more urgent to insure against sickness and its costs than to insure against death. Sickness may disrupt the financial status of the family more than death does.

Let us consider for a moment the spread of the various forms of group medical practice which is still in progress. These developments, which tend to combine "packaged bargains" in medical care with extensions in the medical services to be rendered and with the cooperation of teams of specialists carry potentials for further modifications in patient-personnel relations.

Finally, through the instrumentality of the federal government, increasing amounts of medical care for growing segments of the population are being covered and measurably controlled on a national or state basis. Certain appraisals of the medical care which, at present, is government-sponsored in the United States have already moved about halfway toward some form of group responsibility for the health service of the population.

In summary, I have saluted the medical profession for what it is now able to do for the health and welfare of all of us as potential patients. We are somewhat cognizant of a great lag between what actually is done and what could be done for patients by full use of the medical potentialities now available. We, the public, are dissatisfied with present medical and hospital practice, and there are mounting pressures for improvements. The improvements may come by means of the better application of existing medical knowledge and skills, although it is known that the medical profession will meet with substantial opposition on the part of some potential patients. The lag between what patients actually get and what they might receive in medical care will be slowly overcome; however, it can be boldly assumed that systematic study and research on the social phenomena of medical practice will speed the orderly progress of staff-patient relationships somewhat.

I have cited six broad changes in the social order that have at least an indirect bearing on staff-patient relationships: population mobility, general sophistication, commercialization of the professions, shifts in age composition and disease prevalence in the populace, changes from a religious-philosophical toward a scientific orientation, and the growth and spread of organized pressure groups.

I have also identified five more specific changes within medical institutions and in medical practice: expansion of equipment and capital investment, growth of institutionalization, increase of specialization (of both types), with sharpening potential for apportionment of blame, expansion in the concept of patient care, and the rapid growth of prepayment plans, group medical practice, and the greater participation of the government in the provision of medical care.

Amid such a flux of trends both outside and inside the medical institutions, is it any wonder that personnel-patient relations should be somewhat unsettled or that the professional workers in the field of health, caught in these crosscurrents, should be concerned about what steps to take and in what order?

In conclusion, one thing seems fairly certain. There exist no easy panaceas and simple gadgets that can insure full harmony of personnel and steady progress in health care. Two cautions should be clear to everyone. First, the solutions of yesteryear are insufficient to cope with the problems posed by our changing times. Second, the "magic" of our public-relations gimmicks is too superficial to resolve the deeper issues. It is recommended that our medical leadership examine systematically, and with professional aid, the ways and means by which medical practice fails to keep pace with changes in the social order and to consider the potentials of social research and planned experimentation for overcoming the prevailing "lags."

CLINICAL SCIENCE

TISSUE MAST CELLS

Edwin R. Fisher, M.D., Pittsburgh

During the past few years much information has accumulated concerning the physiological and pathological significance of tissue mast cells. It is more than of historical interest to note that these cells were first clearly described by Ehrlich in 1878.[1] Their abundance in connective tissue which he considered to be "well-nourished," as observed with chronic inflammation, prompted the designation "Mastzellen" (well-fed cells). Ehrlich also proposed that the granules of the mast cells, which exhibit a strong affinity for basic dyes and the property of altering the original color of the dye (metachromasia), represented nutrient for the connective tissue. In the light of this hypothesis, as well as the great interest recently demonstrated in the connective tissue and its purported disorders, it is not surprising to learn that the mast cells have been considered to play a significant role in fibrillogenesis, particularly in the elaboration of connective tissue matrix or ground substance. Although there is suggestive evidence which indicates that the tissue mast cell may participate in this phenomenon, certain considerations obviate unequivocal acceptance of such a proposal.

Role of Mast Cells

I have observed that mast cell depletion after the administration of compound 48/80, a condensation product of p-methoxyphenethylmethylamine and formaldehyde, does not quantitatively or qualitatively influence collagen formation resulting from the subcutaneous injection of carrageen in the rat. Furthermore, both connective tissue and amorphous ground substance are apparent in the embryo before tissue mast cells are perceptible. The distinct

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histochemical and chemical differences between ground substance and the granules of tissue mast cells might also be considered as evidence against such a relationship. Riley [2] has proposed an alternative hypothesis suggesting that the hyaluronic acid secreted by connective tissue cells is removed by the mast cells and stored after their conversion to the sulfated form. Although this interpretation satisfies some of the objections noted above, more supportive evidence appears warranted. Thus, it becomes apparent that Ehrlich's original views concerning the function of the mast cells, although not disproved, must, at least for the time being, be regarded with some reservation.

On the other hand, there is conclusive evidence that the tissue mast cells contain heparin,[3] histamine,[4] and serotonin,[5] the latter as yet identified only in the mouse and rat. Again, however, the biological significance of these substances insofar as mast cell function is concerned remains unsettled. The recognition by Holmgren and Wilander [3] that the tissue mast cells possess heparin was supported by their studies relating a high heparin content to tissues replete with mast cells. This finding appeared compatible with the prior observations of Jorpes [6] and Lison.[7] The former identified heparin as a highly sulfated acid mucopolysaccharide, and the latter related metachromasia to this chemical configuration. Such information provided a histochemical basis for the metachromasia of the granules of the tissue mast cells. The subsequent demonstration that a mast cell tumor obtained from a dog contained 50 times more heparin than the animal's own liver [8] added further confirmation to the observations of Holmgren and Wilander.[3]

It also emphasized the inappropriateness of the term heparin for the natural anticoagulant of the blood. Unfortunately, the discovery of the heparin content of mast cells led many to assume that the mast cells were the source of a naturally occurring anticoagulant, particularly since mast cells by their predilection for adventitial sites were in an opportune position for such an activity. Critical analysis of the data on which this assumption was based strongly indicates, however, that the heparin of tissue mast cells is not normally involved in maintaining the fluidity of the blood. The heparin molecule appears too large to enter the circulation directly through venous capillaries and more probably is first trapped in the tissues, to be subsequently removed by the lymphatics. Of more significance are the studies of Riley [2] which indicated that the evidence relating normal incoagulability to the release of heparin from mast cells was obtained from experiments with anaphylactic shock in the dog and that this species appears unique in exhibiting altered blood coagulation during this state. Since drainage from the liver, which represents the shock organ of the dog, occurs directly into the thoracic duct, altered coagulation might be expected, whereas in other species drainage occurs by way of other lymphatic routes.

Recent observations revealing a marked reduction of mast cells in the intima and subintima of large arteries with atherosclerosis has prompted the suggestion that the release of heparin by the mast cells may provide for the degradation of lipoprotein and the deposition of insoluble lipid.[9] This highly provocative observation merits confirmation. It is germane to note, however, that heparin has the converse effect on atherogenesis in the rabbit and that mast cell depletion in the rat has failed to influence the susceptibility of this species to atherosclerosis.[10]

The discovery by Riley and West [4] that mast cells contain histamine represents another advance in our knowledge of the mast cell. No evidence has been presented, at the time of writing, which might relate the release of this substance to a physiological function of the mast cells. On the other hand, information indicating a histamine–mast cell relationship has been obtained from pathological states. A "triple response" can be obtained in the skin of patients with urticaria pigmentosa, a cutaneous and often systemic disorder characterized by deposits of tissue mast cells. The presence of histamine within mast cells has been further substantiated by the demonstration of histamine in mastocytic tumors of dogs and by the use of agents which produce a release of histamine and an eventual disruption of the mast cells.

The role of the mast cell in inflammation appears to have been unduly neglected, particularly in the light of the histamine content of these cells and their well-recognized abundance in inflammatory processes. Since much of the vascular alteration of inflammation has been attributed to the effect of histamine or histamine-like substances, one might suspect that the tissue mast cell may be the source of such material. It does appear noteworthy, however, that mast cells appear most prominent in chronic inflammation, rather than in the acute stages of this process when the vascular phenomena are most evident.

Much attention has been directed toward the significance of mast cells in neoplastic growth, particularly in relation to their infiltrative properties. Conclusive evidence that the tissue mast cells play a significant role in this regard, however, remains to be elucidated. It is to be noted that there is a paucity of studies concerning this relationship in human neoplasms. Injection of heparin has failed to influence the progression of neoplastic changes observed in precancerous dermatoses of mice.[2]

Recently two examples of leukemia of the tissue mast cell type have been recorded. In both instances, their differentiation from leukemias of the mast leukocyte or blood basophil type was emphasized. In one patient,[11] pruritic, erythematous eruptions of the skin were observed similar to those noted in urticaria pigmentosa, although mast cell infiltrations of this structure were not apparent. In the other,[12] dermal lesions were evident which, when stimulated, resulted in the formation of urticarial wheals. Unfortunately, no mention of the microscopic appearance of the cutaneous lesions was made. These cases are of extreme significance, since at least in the first instance cited there is suggestive evidence that the leukemic mast cells in the blood or leukemic deposits in the tissues were "functioning." Although these cases do not resemble classic urticaria pigmentosa, there appears to be sufficient similarity to suggest that *perhaps tissue mast cell leukemia may represent a* variation of this disorder.

Comment

It becomes apparent from this that great advances in the basic knowledge of tissue mast cells have taken place since their recognition as distinct cellular elements by Ehrlich in 1878. Convincing evidence concerning their biological function, however, is often lacking. Further, many interpretations in this regard appear highly teleological. Much of the difficulty in the resolution of this problem would appear to reside in the transfer of experimental findings obtained from one species to another, as indicated above. There not only are pertinent anatomic dissimilarities between species but also differences in the tissue mast cells per se, as evidenced by divergent tinctorial reactions, response to histamine liberators, and indeed different biochemical composition as well as possibly other parameters of structure and composition which may be species-significant. It appears that the relationship between blood mast cells or mast leukocytes and tissue mast cells, long held as distinct entities, largely on morphologic grounds, is worthy of reevaluation. Recent studies have indicated similarities in these cell types with regard to their heparin content as well as their reaction to histamine liberators. Lastly, it does not appear irrelevant to consider that it might be more significant to focus attention on the depleted mast cells of tissue rather than on those with identifiable, intact granules. This impression is based on the supposition that the well-granulated mast cells observed in tissue sections may represent "storage" rather than secretory forms. Studies that use the histamine liberators should be of value in this regard. The significance of this assertion becomes apparent in the interpretation of alterations of mast cell populations in pathological states. Does a paucity of mast cells indicate that these cells have actively elaborated their contents, or does it reflect a true deficiency state? We are faced, as is so often the case in biological problems, with the proverbial "chicken and egg" dilemma, which may actually in large part reflect the dilemma or riddle of the tissue mast cell.

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NOBEL PRIZE.—Dr. Fritz Lipmann came to the Massachusetts General Hospital in 1941 as Research Chemist, later to be made Head of the Biochemical Research Laboratory and Harvard Medical School Professor of Biological Chemistry at the Massachusetts General Hospital. Here he continued his work on enzymes, begun years before. In 1953 he received the Nobel Prize in Physiology and Medicine, "for his discovery of co-enzyme A and its significance in the intermediary metabolism." (The Nobel Prize for 1953 was divided between Dr. Lipmann and Dr. H. A. Krebs of England.)—N. W. Faxon, The Massachusetts General Hospital 1935-1955, Cambridge, Mass., Harvard University Press, 1959, page 230.

THE JOURNAL
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NORTHWESTERN UNIVERSITY MEDICAL SCHOOL, 1859-1959

MORE than 400 medical colleges were organized in the United States during the 19th century. The state of Illinois claimed 39, of which several were diploma mills or other forms of commercial venture. Only three of the original group have continued. The reform in medical education that followed the Flexner report of 1909 was responsible for the abolition of many of this number. One medical college that has held fast to its avowed function for 101 years was founded by a high-minded and dedicated pioneer band, affiliated originally with Lind University in Chicago. The college subsequently became the Northwestern University Medical School. Its centennial is being celebrated this year.

Five of the seven physicians who planned the new school more than a century ago were active or recent members of the faculty of Rush Medical College, which had opened its doors to students 16 years earlier. Dr. Nathan Smith Davis was probably the best known of the band and is believed to have exerted the greatest influence. He assumed teaching responsibilities in the new school subsequently as Professor of the Principles and Practice of Medicine. His ideas on medical education were advanced and imaginative. They were even considered radical by some.

The original faculty agreed to serve without pay for the first three years. A six-month term of instruction for each of the three years was planned for the students. This was double the term of residence required by other schools at that time. These facts and many others are ably presented in a history of Northwestern University Medical School prepared by Leslie B. Arey,[1] Emeritus Professor of Anatomy, in anticipation of the centennial of the school.

The first two years of the Medical College were completed as a unit of Lind University, which was soon to become Lake Forest College. The Illinois Medical Society, founded in 1840, was invited to appoint a committee of two who would be charged with the responsibility of attending the students' examinations and who would vote at graduation on their qualifications for the degree of Doctor of Medicine. Mercy Hospital provided clinical facilities in the early years of operation. The faculty of the school agreed to provide professional service gratis to the hospital in return for the affiliation.

Dr. Davis reported at the first annual session that there is "a sincere desire on the part of the faculty to put into practical operation a system of medical college instruction more in accordance with sound educational principles, and better adapted to the present state of the science and art of medicine, than that which has long been adhered to by the medical schools of this country." The speaker recounted the defects of medical education then in existence as he sensed them. He urged the adoption of several recommendations proposed by the American Medical Association and that the reform measures be subjected to a fair test. Thus, two significant principles were apparent a century ago. The curriculum of Northwestern University Medical School was to constitute a new and progressive program of medical education. Second, the American Medical Association had evidenced deep concern in the then current deficiencies of medical education. The Association advanced constructive criticism to improve the first and vital stage in the professional career of the physician.

Arey believes that the role played by Davis in curriculum reform was associated with his earnest desire several years earlier to establish the American Medical Association. The prime purpose for creating the Association was the advancement of undergraduate medical learning. Davis became the first editor of THE JOURNAL in 1883 at the age of 66 years and continued in this capacity for more than five years. It is apparent that the imagination displayed by Davis in the organization of the American Medical Association is interwoven with the establishment of Northwestern University Medical School. They provide an outstanding example of vision and capacity for leadership. The American Medical Association honored him, as their President; Northwestern honored him as the Dean of the Medical School.

During the era that followed the opening of the medical college, the financial panic, the Civil War and other socioeconomic forces prompted the cancellation of the affiliation with Lind University. It seemed prudent then to adopt the name Chicago Medical College, an appellation which the institution carried until 1870. At that time the school entered into an alliance with Northwestern University as its medical department. The union became firmer year by year and led to the development of one of the strongest units of this outstanding American university on the shore of Lake Michigan. A new building, constructed for the school, was just outside the area of devastation of the Great Fire of 1871.

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[1] Arey, L. B.: Northwestern University Medical School, 1859-1959, Chicago, Northwestern University Press, 1959.

There are several items that may be submitted as documentary evidence of the pioneering position in medical education assumed by the college. A four-weeks "Practitioners' Course" was started in 1880, the same year that a similar postgraduate course was started at the University of Pennsylvania School of Medicine. Training in the use of the microscope was required of medical students in 1871. Two of the textbooks that were recommended in that year included Gray's *Anatomy* and Virchow's *Cellular Pathology*. The quality of premedical education, the institution of a graded curriculum, and the coordination of didactic and hospital instruction were other evidences of advanced thinking and practice of that era. The medical college was the first to embrace each of the several features of the recommendations advanced by the Cincinnati convention (1867) which became later the accepted principles of medical pedagogy throughout the land. In fact, the college anticipated these reforms by eight years, and it was Davis who induced the convention to advocate them.

During the waning years of the 19th century, the medical school was prominent in attracting teachers and students of international renown. These included such illustrious men of medicine as Drs. Charles H. Mayo, Isaac A. Abt, Franklin H. Martin, Frank Billings, Howard J. Ricketts, Arthur E. Hertzler, Joseph B. DeLee, and John B. Murphy. Beginning in 1893 juniors and seniors were urged to pursue research in addition to the prescribed curriculum. Approved courses were offered to groups of students with special laboratory and clinical instruction. More than 70% of the students chose one or more elective courses. This practice has continued up to the present. One year of college preparation only was required for admission in the first quarter of the 20th century. Bedside teaching was stressed, and a one-year internship after graduation was required before the M.D. degree was conferred. The latter regulation was not abandoned until 1951.

The present modified Gothic structures on the near north side of Chicago were begun in 1925. They were built by generous funds provided by gracious friends. These included Mrs. Montgomery Ward, in memory of her husband, Mrs. Margaret G. Morton, in memory of her husband, and the estate of Dr. and Mrs. Wallace C. Abbott, founder of Abbott Laboratories. The teaching hospitals affiliated with the school are Chicago Wesley Memorial, Children's Memorial, Evanston, Passavant Memorial, and Veterans Administration Research Hospital. A massive medical center stands as a tribute to its founders, a citadel for medical education, and a haven for the sick. The destinies are in the hands of a competent faculty under Dean Richard H. Young, who in 1948 succeeded to this post after his classmate, Dr. J. Roscoe Miller, was appointed President of Northwestern University.

What of 1960? The template of transition of a century earlier is being applied. A comprehensive change in the curriculum has just been announced by the dean and the president. The revised curriculum will eliminate the sharp division between premedical and medical studies. It will introduce in the liberal arts college courses that are more intimately related to the study of medicine and in the same stroke will bring the humanities into medical instruction. The traditional seven or eight years of college and medical school will be reduced to six years for a group of 25 students selected directly from high school. Premedical courses in a concentrated measure and in graduated sequence will be pursued the first two years. About one-third of the time during the premedical period will be devoted to the physical and biological sciences, one-third to the behavioral sciences, and one-third to the humanities. The program will include also a rearrangement of the medical school curriculum for all other students and the introduction of noncredit required courses, given in seminar form, in the humanities.

An initial grant from the Commonwealth Fund will provide financial support for faculty members for the first three years. They will devote sufficient efforts to exploit the new courses in the program. The fund has also pledged a modest sum toward a new building to house special facilities and to provide additional clinical and research space for the Medical School Departments. Unit laboratories will be constructed to accommodate small groups of students. The units will serve as a point of identification with the medical school and will provide an opportunity for independent laboratory and research work if desired. These significant statements attest to the fact that Northwestern University Medical School is in the advance guard of reform in medical education in 1960 as it was in 1860.

It is hoped that the reduction in years for the educational program will attract scientifically oriented students who may be discouraged now by the long years of preparation for medicine. The shorter program should increase the interest of such students in a combined program for the Ph.D. and M.D. degrees and thus insure a supply of persons needed badly for careers in academic medicine. A number of students will devote much of their elective time to research work. In some instances, advantage will be taken of the opportunity to qualify for a Master's degree prior to the Doctorate in Medicine. A progress report 10 years hence undoubtedly will recount these and other accomplishments of Northwestern's mission in medicine.

THEODORIC ON SURGERY

"Here begins the Surgery edited and compiled by the Dominican, Brother Theodoric, Lord Bishop of Cervia." The seven books of surgery by Theodoric were published about 1267 A. D. The most recent translation is by Campbell and Colton.[1] It is noteworthy that several of the precepts of the practice of this specialty were subject to test and found valid seven centuries ago. The translators note that the teachings of Theodoric were astonishingly similar to those of Halsted. "There is no need . . . to be rash or daring, but let them be foresighted, gentle and circumspect, in order that, with the greatest deliberateness and gentleness they may operate under all circumstances with what gentleness they can, especially around cerebral membranes, sensitive parts and other ticklish places . . . All the things that are necessary to the art cannot be included in books, many of these frequently happen to the operator, and cannot easily be foreseen. Surgeons must need be well-read, for even though they be experienced, they will frequently fall into error and confusion, and I can scarcely think that anyone can understand surgery without letters."

The father, or at least the spiritual leader and professional teacher, of Theodoric was Hugo, a surgeon as skilled and learned as his pupil. Hugo did not prepare a treatise on surgery, but Theodoric attributes to him the following teachings. "In the first place the lips of the wound and all about the wound should be abraded or debrided; then the wound should be completely cleaned of fuzz, hair and anything else, and let it be wiped dry with fine lint soaked in warm wine and wrung; and thus the lips of the wound may be reunited as well as possible in accordance with their original healthy state; and having made compresses of fine and clean lint soaked in warm wine and placed upon the wound so as to fit, let it be bound up with a light bandage in such a way as the reapproximation of the wound edges cannot be disturbed at all—and, just as we have said before, do not undo the dressing until the third, fourth, or fifth day if no pain occurs."

Theodoric anticipated contemporary Russian surgery, as follows: "If a nose has been sliced by a sword or other weapon so that it is hanging on . . . you should be both circumspect and cautious. Replace the nose very cautiously in its proper position, so that each part is matched to the part from which it was separated . . . and having taken stitches in suitable places, let each part of the nose be sewed to its corresponding part."

Most of the fractures and dislocations encountered currently in traumatic surgery are discussed and therapy recommended. "When vertebrae of the back are completely dislocated, the result is inevitably fatal. If the dislocation . . . should be directed toward the interior of the chest, there is no ingenious method for treatment. . . but the type which is displaced posteriorly is called gibbous . . . sometimes the vertebrae of the spine had been separated posteriorly . . . in such a case then the physician ought to make ready two long splints which extend from the scapula, to the buttocks . . . and bind the patient down with white bands from below the arm pits to the shoulder, and lower down, over the hips and around the thigh."

Volume 2 contains discussions of fistula, goiter (bocium), abscesses, hemorrhoids, wens, nodules, and gout or the arthritic affection. Noli-me-tangere (rodent ulcer) was cured by "the blood of some person who has suffered the same disease, for this is a special treatment for the affection, and infallible." Herpes estiomenus, also known as lupus or the self-devourer (L., estiom), was treated by cautery. The several types of imposthumes (sing.. imposthume), internal and external, were described in detail. The objective in the treatment of a solid testudo was to exercise care in removal of the tunic. If the testudo was liquid the sanies was to be evacuated. "Often times there occurs certain superfluity in some people which is commonly called lipoma (nata). . . . It is not accompanied by pain, heat, nor pulsation. And perhaps it is for this that it grows so large that it surpasses all other superfluities of the body. . . . And be careful not to incise a lipoma which is dark in color and of little sensitivity, since this is a cancerous imposthume." Figs in the anus were treated by poulticing.

Berry concludes the foreword to the first volume with these words: "All in all for those interested in the history and development of surgery, this volume is of great interest, and as one realizes the extent of knowledge that was available in those days and the terrific conditions with which the physician had to contend, one cannot but feel a sense of humility and deep thanks to this small and steadfast group of educated surgeons who continued to carry forward the torch of surgery against almost overwhelming odds. It is indeed a wonder to us today that they were so successful."

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[1] The Surgery of Theodoric, translated by E. Campbell, M.D., and J. Colton, M.A., New York, Appleton-Century-Crofts, Inc., vol. 1, 1955, vol. 2, 1960.

THE DEAN AND SHERLOCK HOLMES

"On trains and planes, in motels and hotels, when traveling on business in connection with the development of the new medical center at West Virginia University," the Dean of the Medical School prepared a delightful enchiridion on Sherlock Holmes.[1] E. J. Van Liere is not unique as a doctor who enjoys mystery stories. In recent years television has been responsible for a change in medium of transmission of the thriller from author to doctor. Prior to the creation of this neoteric device of communication, physicians found a pleasant means of escape from the hour-to-hour and day-by-day travail of practice by the simple procedure of reading mystery stories. L. J. Henderson, Doctor of Medicine, biochemist, and proponent of the D'Ocagne nomogram, readily boasted of a modest collection of mystery stories on his bedside table. He had no hesitation in admitting that a cleverly fabricated tale of crime and corruption was diverting as well as soporific. Now the dean of a new medical school admits membership in the organization of medical devotees of yarns that reveal the answer on the last page.

The composite of Sherlock Holmes refers only to the medical aspects of the narratives of A. Conan Doyle. These are sufficient to fill a small volume. The extent of the medical references is not surprising. Dr. Watson, physician, surgeon, neurologist, and psychiatrist, was a constant companion of Holmes's, although not often of vital help in solving a case. Dr. Watson was also interested in zoology and other biological sciences. He spoke with authority when he urged fasting or a light meal for intense mental activity needed to effect a solution ("The Adventure of the Norwood Builder"). The cerebral physiologist might not agree, although a heavy meal undoubtedly can make one physically lazy if not mentally inhibited. In the "Adventure of the Devil's Foot" Watson implies that the male is physiologically superior to the female. Actuarial data compiled by life insurance companies tend to negate such a premise. "Sherlock Holmes was a man who seldom took exercise for exercise' sake ('The Adventure of the Beryl Coronet'). He looked upon aimless bodily exercise as a waste of energy."

"We may think of the faithful Doctor Watson answering a call, perhaps late at night, his stethoscope concealed in his hat, and his trusty medical bag filled with the acceptable drugs. We can picture him further, riding along in his hansom—the lights of which shone dimly through the fog—rattling over the cobblestones of the old London streets, and carrying on the tradition of his noble profession"—or on his way to help Mr. Holmes with his latest unsolved assignment. It may be somewhat simpler to operate a remote control switch in order to view the latest mystery, but while something can be gained by this device, something also is lost when the tales of Doctor Watson and S. Holmes are seen and not read.

ACCEPTANCE OF RESPONSIBILITY

Medical training in the postgraduate years is discussed by Stanley E. Dorst in this issue of The Journal. "Dilemma" is the title of communication, but it might have been captioned "Who Is to Do It," "Whither Away," or "Why Wasn't Something Done About It Earlier?" Several pertinent facts are emphasized and several crucial questions posed. The Flexner Report of 1909 is placed in proper perspective. The recommendations of this report were responsible for the transition in predoctoral medical education from poor or mediocre to the pinnacle of excellency. But the current pinnacle in predoctoral medical education that has been reached may be likened to a single peak in a mountain range. There are other peaks that must be conquered in the struggle for attainment. Reference is made specifically to postdoctoral medical education. The provision of an adequate number of interns and residents for hospitals throughout the country is an enigma that must be solved by studied and careful planning. Surely a portion of the solution will be intimately related to the staff of visiting physicians who are willing to sacrifice time and thought in training the members of the house staff. Equally important in postdoctoral medical education is a critical inquiry into the mission and function of the several specialty boards. Such critical inquiry, according to Dean Dorst, must come from within, i. e., from the responsible officers of the governing bodies of the specialty boards. Dorst speaks from experience. He has been a member of the advisory council to the specialty boards for a number of years. Unfortunately, he found, this counseling has not led to integrated action. Until this deficiency is corrected, the multiple mission of the boards will not be fulfilled.

Nor are the officers of the specialty boards solely responsible for scrutiny and analysis. Each and every member of the American Medical Association should be aware of such matters which are of concern either because of certification in one of the specialty boards or because practice in the community by the specialty board member inevitably affects physicians who are not specialty board members. It is axiomatic that an enlightened program of specialty boards will benefit physicians as well as patients. Organized medicine through the American Medical Association assumed a major role in the correction of deficiencies in pregraduate medical education early in the century. Organized medicine once more is called on to give serious thought to these matters, to offer suggestions for correction, and to be prepared eventually to implement any thoughtful action deemed necessary.

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[1] Van Liere, E. J.: Doctor Enjoys Sherlock Holmes, New York, Vantage Press, Inc., 1960.

COUNCIL ON OCCUPATIONAL HEALTH AND COUNCIL ON MEDICAL SERVICE

The following report, prepared by the Committee on Medical Care for Industrial Workers, a joint Committee of the Council on Occupational Health and the Council on Medical Service, has been approved for publication by the two Councils.

B. Dixon Holland, M.D., *Secretary*
Council on Occupational Health
Mr. George W. Cooley, *Secretary*
Council on Medical Service

SURVEY OF PHYSICIANS' SERVICES IN SMALL PLANT OCCUPATIONAL HEALTH PROGRAMS

The Committee on Medical Care for Industrial Workers, a joint Committee of the Council on Occupational Health and Council on Medical Service of the American Medical Association, has long been interested in the provision of occupational health services to employees in small plants, and in 1959 conducted a survey of physicians' services provided to small plant occupational health programs. "Small plants," defined for purposes of this survey as industrial, business, and commercial establishments employing fewer than 500 employees, comprised some 99% of all establishments and employed four-fifths of the labor force in the United States as of the beginning of 1959. The provision of occupational health services to this large number of employees is important, and the Committee has encouraged the development of occupational health programs suitable for adoption by most small plants.

A review of various early experimental and of some current programs revealed that they had failed to provide the impetus for greatly needed expansion. The Committee, therefore, decided that a reappraisal of the arrangements and methods by which such services could be made available to small plants was essential. It was evident, too, that the pattern which had developed in providing occupational health services to employees in large establishments, with emphasis on full-time salaried physicians, had obscured the role private practitioners could play in providing such care for the many thousands of small groups of employees.

Physicians in private practice (as distinguished from industrial medical practice) have never fully realized the contribution they could make to occupational health. The fact that many physicians are not contributing to occupational health programs is explainable, in part, by the connotation to them of the term "industrial medicine," by their lack of interest in acquiring the necessary special knowledge to supervise occupational health programs, and by their unfamiliarity with certain aspects of workmen's compensation laws. These factors, however, will not deter the physician who recognizes the challenges and satisfactions of this type of practice and is aware of the role, scope, and objectives of an occupational health program and the part he can play in them.

The importance of the private practitioner in instituting and developing occupational health services for employees in small plants is clearly shown in this survey. The findings which appear below should be of interest to all physicians and should serve to stimulate greater interest in, and awareness of, the potentials of small plant occupational health services.

Methods and Objectives of Survey

A list of 1,050 physicians known to be providing occupational health services was obtained from 40 states and the District of Columbia. In February, 1959, questionnaires were mailed to these physicians, requesting them to supply the Committee information on the occupational health services they provided to employees in small plants. By April about 250 replies had been received. Two hundred of these contained sufficient data to be incorporated in this report.

The Committee did not attempt in this survey to get a cross-section of the types of occupational health services provided by physicians in private practice (as distinguished from full-time, salaried industrial physicians) or the methods they used, or to obtain a representative sample of all physicians in private practice providing such services. The pri-

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Committee members are Frank J. Holroyd, M.D., Chairman, Princeton, W. Va.; Gilbeart H. Collins Jr., M.D., Chicago; John F. Conway, M.D., Clovis, N. M.; Thomas J. Danaher, M.D., Torrington, Conn.; W. Benson Harer, M.D., Upper Darby, Pa.; Edwin P. Jordan, M.D., Charlottesville, Va.; Melvin N. Newquist, M.D., West Cornwall, Conn.; Leo Price, M.D., New York City; and Mr. Murray Klutch, Research Associate, Chicago.

mary objective of the Committee was to explore, on a pilot basis, the validity of its opinion that (1) physicians in private practice are, to some extent, already providing occupational health services, and (2) this experience can help other interested physicians by showing them what services they could offer.

TABLE 1.—*Number of Small Plants Served by Physicians Practicing Alone*

Physicians, No.	Plants Served, No.	Plants, No.
41	1	41
33	2	66
20	3	60
12	4	48
5	5	25
5	6	30
1	7	7
3	8	24
3	9	27
4	10	40
1	12	12
2	15	30
5	20	100
2	25	50
1	100	100
138		660

The Committee undertook this survey on the assumption that the physician in private practice would help meet existing needs in this field if he were made aware of the opportunities, responsibilities, and obligations involved.

Findings of Survey

One hundred thirty-eight of the 200 usable responses received from physicians serving small plant occupational health programs were from physicians practicing alone. Sixty-two were from physicians who were members of groups that provided such services. A great variety of small plants were designated as having occupational health programs.

TABLE 2.—*Number of Small Plants Served by Physicians in Group Practice*

Groups, No.	Plants Served, No.	Plants, No
12	1	12
12	2	24
8	3	24
5	4	20
3	5	15
4	6	24
3	7	21
2	10	20
1	12	12
1	13	13
2	15	30
2	20	40
2	25	50
1	30	30
1	35	35
1	50	50
1	175	175
1	200	200
62		795

Table 1 reveals that 138 physicians, practicing alone, provided occupational health services to 660 small plants. Forty-one physicians served only one small plant each. Ninety-six served as many as 25 small plants each. More than 45% of the physicians served from two to four plants each. (All data in the tables were derived from a Survey of Physicians' Services in Small Plant Occupational Health Programs, conducted by the Committee on Medical Care for Industrial Workers, February, 1959.)

Table 2 shows that 62 groups of physicians served 795 small plants. These groups, consisting of from 2 to 20 physicians, served from 1 to 200 small plants each. Only 51 of the 62 groups provided information on the number of physicians in their groups; the total number in the 51 groups was 303.

TABLE 3.—*Distribution of Employment in Small Plant Occupational Health Programs Served by Physician Practicing Alone*

Plants, No.	Total, %	Employment Size	Employees, No.
39	11.1	<25	507
36	10.2	25-50	1,332
87	24.8	51-100	6,525
65	18.4	101-200	9,750
58	16.5	201-300	14,500
31	8.8	301-400	10,850
36	10.2	401-500	16,200
352	100.0		59,664

Table 3 provides a breakdown of the small plants by number of employees for those occupational health programs served by physicians practicing alone. Information on employment was provided for 352 establishments with 59,664 employees.

Table 4 provides a breakdown of the small plants by number of employees for those occupational health programs served by physicians in group practice. Information on employment was provided for 199 establishments with 43,245 employees.

Table 5 gives the dates of origin of small plant occupational health programs served by physicians practicing alone and programs served by physicians in group practice. Over 40% of the programs in each group originated since 1951.

TABLE 4.—*Distribution of Employment in Small Plant Occupational Health Programs Served by Physicians in Group Practice*

Plants, No.	Total, %	Employment Size	Employees, No.
5	2.5	<25	65
15	7.5	25-50	555
23	11.6	51-100	1,725
65	32.7	101-200	9,750
36	18.1	201-300	9,000
26	13.1	301-400	9,100
29	14.5	401-500	13,050
199	100.0		43,245

Table 6 indicates on whose initiative the small plant occupational health program was begun. In this order of frequency, the following groups took the initiative for instituting occupational health programs (*a*) management, (*b*) physicians and management, and (*c*) physicians alone. In groups *b* and *c* such initiative has usually resulted from community interest and stimulation as reflected in meetings sponsored by local business groups, medical society committees on occupational or industrial health, and other organizational efforts.

Table 7 lists the types of services provided by the 138 physicians practicing alone and serving occupational health programs of small plants. The three leading types of services are (1) care of workmen's compensation cases, (2) preplacement examinations, and (3) return-to-work examinations. The table also indicates the locations where such services are performed. Most of them are rendered in the offices of the physicians, although the plant premises are used to a considerable extent. Other services mentioned by physicians included the administration of influenza and poliomyelitis vaccine, executive health examinations, and teaching of first-aid courses. These were in addition to the rendition of first-aid and palliative treatment for cases of minor illness or injury while the employee was at work.

TABLE 5.—*Dates of Origin of Small Plant Occupational Health Programs*

Served by Physicians Practicing Alone			Served by Physicians in Group Practice		
Date	Plants, No.	Total, %	Date	Plants, No.	Total, %
Prior to World War II ..	81	25.1	Prior to World War II ..	32	20.4
1941-1945	48	14.8	1941-1945	20	12.9
1946-1950	54	16.8	1946-1950	42	26.7
1951-1955	97	30.0	1951-1955	29	18.5
1956-1958	43	13.3	1956-1958	34	21.5
Total	323	100.0		157	100.0

Table 8 lists the types of services rendered by physicians in group practice. The three leading services are (1) preplacement examinations, (2) care of workmen's compensation cases, and (3) return-to-work examinations. A greater percentage of these services are provided in the offices of the groups than in the offices of the physicians who practice alone.

TABLE 6.—*Initiative Taken in Developing Small Plant Programs, and Number of Plants Served by Physicians Practicing Alone and Those in Group Practice*

Group	Physicians Practicing Alone	Physicians in Group Practice
Management	199	42
Physicians and management	85	9
Physicians	45	7
Employees	4	..
Miscellaneous (e.g., insurance co's.)	8	2
	341	60

The questionnaire requested physicians to indicate the average amount of time they devoted each week to the provision of occupational health services to small plants. Ninety-one of the physicians practicing alone and 26 of the group practices provided specific answers. The replies reveal a considerable variation in time spent. About 50 additional replies indicated "great variation" and six indicated "seasonal variation" in the number of hours devoted to these programs. Table 9 contains a breakdown of this information.

Of the 138 physicians practicing alone to provide occupational health services, 35 were on a regular basis (i. e., with definitely assigned hours), 78 were on an on-call basis, and 23 considered themselves as both regular and on-call. Two did not answer.

Of the physicians practicing in the 62 groups, physicians in 18 groups were on a regular basis, physicians in 37 groups were on an on-call basis, and physicians in 5 groups were on both a regular and on-call basis. Two did not answer this question.

Physicians were asked to indicate the number of nurses employed in small plant occupational health programs. Of 204 small plants served by physicians practicing alone, 138 had full-time nurses on duty, 24 had part-time nurses, and 42 had no nurses. Of 74 plants served by physicians in group practice, 48 had full-time nurses, 5 had part-time nurses, and 21 employed no nurses.

TABLE 7.—*Types of Small Plant Occupational Health Services Provided by Physicians Practicing Alone, and Locations Where Services are Rendered*

	Individual Physicians Providing Services	Location of Service Rendered		
Service, Type	(out of 138)	Office	Plant	Other
Preplacement examination	117	88	55	..
Periodic examination	96	58	50	..
Hazardous employment examination	60	35	38	..
Return-to-work examination	108	74	52	..
Care of workmen's compensation cases	118	107	57	24*
Health education and counseling ..	58	19	40	..

* Hospital.

Physicians were also asked to submit additional information on various experiences with these programs, reactions of employees, managements and unions, relationships with other physicians in the community, problems encountered in the development of the programs, and any other information which they considered would be helpful to the Committee. Many such comments were received, and from them certain broad generalizations can be drawn.

On the whole, physicians practicing alone or in groups are satisfied with the occupational health programs they serve and with the relationships they have established through these programs. The reactions of employees, managements, and unions have generally been favorable; where problems were originally encountered, they have gradually been overcome or are being resolved as the programs become better established. A small number of replies listed various problem areas, including the need to gain recognition of the value of occupational health services by management and employees and the need to encourage the expansion of occupational health programs to include more services. A few physicians noted the tendency on the part of employees to request treatment for nonoccupational conditions, which is outside the scope of occupational health programs. Some commented on the unwillingness of some managements adequately to compensate the physician for services to these programs. With a few exceptions, relationships between physicians in the community and those serving small plant programs were described as "satisfactory" or "excellent."

The form in which some of the data were submitted, or their receipt after the analysis was prepared, prevented the analysis of an additional 50 replies. A few of them did, however, contain detailed reports of program operations and descriptions of the services provided. One described a "Small Plant Medical Service" in a New England state in which one physician provides occupational health services to seven small plants. This program is unique in that the physician devotes his entire practice to the provision of occupational health services. He spends from four to eight hours a week at each plant.

Another detailed reply described the operation of an "Employees' Health Service" in a southern state, under which some 18 to 20 thousand state government employees, in small groups, are provided multiphasic screening examinations, first aid, and health counseling.

Summary and Conclusions

The results of the survey confirm the Committee's belief that the physician in private practice, whether practicing alone or in a group, when given the opportunity can provide to employees in small plants the medical services outlined in the statement on "Scope, Objectives and Functions of Occupational Health Programs" adopted by the House of Delegates in June, 1957. The principles outlined in this policy statement can help guide physicians serving small plant occupational health programs. Although most physicians are, in one way or another, concerned with various aspects of occupational health programs in caring for employees as patients, it is apparent that relatively few concern themselves with the total program of occupational health and with the attendant responsibilities and opportunities.

TABLE 8.—*Types of Small Plant Occupational Health Services Provided by Physicians in Group Practice, and Locations Where Services are Rendered*

Service, Type	Physicians in Group Practice Providing Services (out of 62)	Location of Service Rendered		
		Office	Plant	Other
Preplacement examination	62	59	11	..
Periodic examination	49	37	16	..
Hazardous employment examination	32	27	7	..
Return-to-work examination	53	45	10	..
Care of workmen's compensation cases	58	38	8	9*
Health education and counseling	24	15	12	..

* Hospital.

TABLE 9.—*Average Amount of Time Spent Per Week by Physicians Providing Occupational Health Services to Small Plant Programs*

Number of Hours to Small Plant Programs	Physicians Practicing Alone	Physicians in Group Practice
<1	2	..
1-2	21	4
3	9	1
4	14	2
5	11	6
6	..	3
7-8	12	2
9-10	9	6
14	1	1
15	7	..
20	2	..
25-35	1	..
40	2	1

The physician in private practice, if he is made aware of the special occupational health problems of small plants or if he is interested in enlarging the scope of his practice, will find that he can supervise and administer a small plant occupational health program, for office employees or assembly-line workers. Basically, the physician should possess a knowledge of the working environment, equipment and processes and their physical and mental demands, and the physical and mental abilities of the prospective employee or the person who is already on the job. He should know, or seek advice on, how certain environmental factors (including illumination, noise, temperature, humidity, dust, chemicals and other agents) affect the performance and general well-being of the individual person. He should be aware of various personnel policies and the role of supervision as they affect the person's relation to, and performance on, the job. He should know the available community resources from which information can be readily secured. He should be prepared to conduct various types of examinations, such as preplacement, periodic, return-to-work, hazardous employment, and preretirement. He should, moreover, be available for whatever health counseling, advice, and guidance employees require or which he considers necessary in a health maintenance program.

Various arrangements and facilities can be utilized by physicians in private practice for serving small plant occupational health programs. For some small plants it may be necessary to advise management to set up a small dispensary in which various types of examinations can be performed and first aid rendered. For other small plants the physician's office can be the center for the supervision and rendition of occupational health services. A part-time or full-time nurse, operating under standard procedures, may be necessary, depending on the particular circumstances and requirements of the specific plant. The physician's office may be so easily accessible to the small plant or office that the services of a nurse may be required for shorter periods of time or not at all.

Many agencies and much reference material are available to the physician to assist and to guide him in supervising or initiating an occupational health program. Agencies include medical society committees on industrial health and occupational health divisions of official public health departments. Numerous periodicals and textbooks are devoted exclusively to various aspects of occupational health programs. Publications and advice can be obtained from several agencies, including particularly the Council on Occupational Health of the American Medical Association.

This survey indicates that physicians in private practice can assist materially in fulfilling the occupational health needs of small plants. It reveals several types of arrangements presently used by physicians in private practice for serving small plant occupational health programs. These arrangements would prove helpful to other physicians in private practice interested in serving such programs. It is hoped that this survey will stimulate interest in occupational health programs on the part of physicians in private practice, to the end that many more will include this type of work in their medical practice.

Selected List of Publications Available from the A. M. A.

Scope, Objectives and Functions of Occupational Health Programs
Guiding Principles of Medical Examinations in Industry
Guiding Principles and Procedures for Industrial Nurses
Occupational Medicine in Industrial Relations
Medical Relations in Workmen's Compensation
The Legal Scope of Industrial Nursing Practice
A Guide for Medical Services for Construction Projects
Guide for Industrial Immunization Programs
Estimation of Loss of Visual Efficiency
A Preliminary Guide for Measuring Work Absence Due to Illness and Injury
A Syllabus on Work Absence
Absence from Work Due to Non-Occupational Illness and Injury

Selected Bibliography

Company Medical and Health Programs (Revised): Studies in Personnel Policy no. 171, National Industrial Conference Board Inc., 1959.

Cooperative Medical Programs—New Solution for Small Companies: Studies in Personnel Policy no. 134, National Industrial Conference Board, Inc., 1953.

Dickinson, W. W.: Small-Plant Medical Service, A. M. A. Arch. Indust. Health, vol. 19, May, 1959.

Health Maintenance for Greater Efficiency: Small Business Administration, Series 16, Oct., 1954.

Health of People Who Work: National Health Council, New York, 1960.

Iowa Industrial Health Survey, 1957-1958: Committee on Industrial Health of the Iowa State Medical Society, J. Iowa M. Soc., Aug., 1959.

Klem, M. C., and McKiever, M. F.: Small Plant Health and Medical Programs, U. S. Department of Health, Education, and Welfare, Division of Special Health Services, Public Health Service Publication 215, Jan., 1958.

O'Connor, R. B.: Analysis of Existing Types of Small-Plant Health Services in Northeastern United States, A. M. A. Arch. Indust. Hyg., vol. 3, Jan., 1951.

COUNCIL ON NATIONAL SECURITY

NATIONAL CIVIL DEFENSE CONFERENCE

The Eighth Annual National Medical Civil Defense Conference will be held at the Americana Hotel in Miami Beach on Saturday, June 11, immediately prior to the opening of the annual meeting of the American Medical Association. The program, sponsored by the A. M. A. Council on National Security and presented by the Medical Department of the United States Navy, will deal with some of the basic and perhaps the most controversial areas of civil defense and survival.

The morning session will be addressed by Dr. E. Vincent Askey, Los Angeles, who will assume office as president of the A. M. A. on Tuesday, June 14. Rear Adm. B. W. Hogan, M.C., surgeon general of the Navy, will open the program.

Clinical aspects of radiation exposure, human responses to confined environments, and casualty care in disasters are the three general topics to be discussed. The first topic will include an exploration of the problem of radiation injury and the current status of medical management, with emphasis on diagnosis, nursing care, and treatment. Current research in the total problem of mass radiation casualties will be discussed during the morning session.

This discussion will be followed by a study of the second topic, the first scientific report of group reaction to isolation and confinement. The report comes as a result of the study of environmental conditions sustained by 97 persons undergoing two weeks of underground confinement.

The afternoon session will be devoted to discussion of the third topic and will stress the importance of community preparedness as the basis for national survival. A film review of recent disasters, with a running commentary on the special medical problems of these situations, will be presented.

Medical units of the Second Marine Division will erect the components of a 60-bed field hospital adjacent to the hotel and demonstrate techniques and ideas for setting up and operating a mobile hospital for the care of mass casualties.

A number of exhibits will support the theme of the conference. Special exhibits will be devoted to bone marrow procedures, blood storage, training techniques, publications, visual aids, and training facilities.

Information pertaining to registration for the conference may be obtained from the Council on National Security, American Medical Association, 535 N. Dearborn St., Chicago 10.

8:00- 9:00 Registration

9:00- 9:05 Call to Order and Introductory Remarks
Harold C. Lueth, M.D., Chairman, Council on National Security, A. M. A.

9:05- 9:15 Welcome Address on Behalf of A. M. A.
E. Vincent Askey, M.D., President-Elect, A. M. A.

9:15- 9:30 Introductory Remarks
Rear Adm. Bartholomew W. Hogan, M. C., U. S. N., Surgeon General, Department of the Navy, Washington, D. C.

SESSION 1–CLINICAL ASPECTS OF RADIATION EXPOSURE: Application of Progress in Research to Patient Care.

9:30- 9:55 Clinical Management of Patients Exposed to Radiation in Disaster
Capt. E. R. King, M. C., U. S. N., Chief, Department of Radiology, United States Naval Hospital, National Naval Medical Center, Bethesda, Md.

9:55-10:10 Nursing Care of the Radiation Patient
Lieut. Commander Lenore Simon, N. C., U. S. N., Head, Nuclear Nursing Division, Department of Nuclear Medicine, United States Naval Medical School, National Naval Medical Center, Bethesda, Md.

10:10-10:35 Procurement, Processing, and Storage of Bone Marrow: Implications for Civil Defense
Capt. George W. Hyatt, M. C., U. S. N., Director, Tissue Bank Department, United States Naval Medical School, National Naval Medical Center, Bethesda, Md.

10:35-11:00 Current Status of Bone Marrow Transplantation: Disaster Aspects
Commander William McFarland, M. C., U. S. N., Chief of Clinical Hematology, National Naval Medical Center, Bethesda, Md.

11:00-11:30 Break

SESSION 2–HUMAN RESPONSES TO CONFINED ENVIRONMENTS: Contributions to our Knowledge of Shelters.

11:30-11:50 Medical Aspects of Shelter Survival
Capt. Harry S. Etter, M. C., U. S. N., Radiological Medical Director, United States Naval Radiological Defense Laboratory, San Francisco.

11:50-12:05 Life in Confined Environments
Capt. Gerald J. Duffner, M. C., U. S. N., Director, Submarine Medicine Division, Bureau of Medicine and Surgery, Washington, D. C.

12:05-12:20 Group Behaviour in Isolation: Antarctica
Lieut. Commander John E. Rasmussen, M. S. C., U. S. N., Coordinator, Neuropsychiatric Research, Bureau of Medicine and Surgery, Washington, D. C.

12:20- 2:00 Luncheon

SESSION 3–CASUALTY CARE IN DISASTERS: Out of its Experiences with Disasters Around the World and in Support of the United States Marine Corps in Amphibious Warfare, the United States Naval Medical Department has Evolved Techniques which are Applicable to Civil Defense Employment.

2:00- 2:40 Disaster: The Past is Prologue
Capt. Clifford P. Phoebus, M. C., U. S. N., Director, Astronautical Division, Bureau of Medicine and Surgery, Washington, D. C.

2:40- 3:00 Techniques of Teaching First Aid and Self Aid for Disasters
Capt. Malcolm W. Arnold, M. C., U. S. N., Director, Professional Division, Bureau of Medicine and Surgery, Washington, D. C.

3:00- 4:15 Local Survival: The Basis for National Survival
Medical units of the United States Marine Corps will demonstrate equipment and techniques applicable to disasters.

COUNCIL ON NATIONAL SECURITY

The name of the Council on National Defense has been changed to Council on National Security, and the new Chairman is Harold C. Lueth, M.D., of Evanston, Ill. Dr. Richard L. Meiling of Columbus, Ohio, is Vice-chairman. The new Chairman of the Council's Committee on Disaster Medical Care is Dr. Carroll P. Hungate, Kansas City, Mo., and the new Chairman of the Council's Committee on Military Medical Affairs is Dr. Reuben A. Benson, of Bremerton, Wash. The following physicians are members of the Committee on Disaster Medical Care: Carroll P. Hungate, Chairman; Wayne P. Chesbro, Berkeley, Calif.; James E. Fitzgerald, Washington, D. C.; Francis C. Jackson, Pittsburgh; Charles L. Leedham, Cleveland; Max L. Lichter, Melvindale, Mich.; Harold C. Lueth, Evanston, Ill.; Frank F. Schade, Los Angeles; Charles W. Steele, Lewiston, Maine; and Charles N. Wyatt, Greenville, S. C.

MEDICAL NEWS

CONNECTICUT

Sesquicentennial for Yale.—The Yale University School of Medicine, New Haven, will celebrate next year the 150th anniversary of its founding with several special events, Dr. Vernon W. Lippard, dean of the school, announced. The anniversary year will open next fall and extend until June, 1961. The first major program in the celebration will come Oct. 28-29 with the regular University Alumni Board Convocation devoted to a review of medical developments, past and present. It was in October, 1810, that the Connecticut General Assembly granted a charter to Yale College for the establishment of the medical school, making it the sixth oldest medical institution in the country. Other events being planned for next year include a scientific meeting, exhibitions (including one on medical art in the Yale Art Gallery), special lectures, and the publication of a history of the medical school.

ILLINOIS

Institute on Medical Teaching.—The Summer Institute on Medical Teaching conducted in 1958 and 1959 at the University of Buffalo will this year be held under the auspices of the Association of American Medical Colleges at the Hotel Moraine in Highland Park, a north shore suburb of Chicago. The conference, June 19-26, will provide an opportunity for medical instructors and specially qualified personnel from education to join in an examination of teaching and learning in medical schools. Included in the presentations, demonstrations, and discussions will be such topics as the nature of learning; the nature of medical students and faculties; the use of lecture and laboratory, ward exercise, and clinical conference, as well as less familiar methods of instruction; the use of tests and other appraisal devices for measuring student performance in a medical school. Attendance at this meeting must be limited. Further inquiry regarding participation should be directed to Dr. Ward Darley, Association of American Medical Colleges, 2530 Ridge Ave., Evanston, Ill.

INDIANA

Pathology Seminar in Indianapolis.—The Indiana Association of Pathologists is presenting its 12th annual seminar in co-sponsorship with the U. S. Veterans Administration Hospital. "Diseases of the Alimentary Tract" will be presented by Dr. Elson B. Helwig, Armed Forces Institute of Pathology, Washington, D. C., May 22, 10 a. m., at the Veterans Administration Hospital Auditorium, 1481 West 10th Street, Indianapolis. Slide sets and protocols are available for physicians who are not members of the association who wish to attend. The available sets will be issued in the order of receipt of applications. A check for $10 should be sent, together with the request for the set, to Dr. Lester H. Hoyt, Secretary, Indiana Association of Pathologists, Methodist Hospital, Indianapolis 7. Members of the medical profession are cordially invited, whether or not they obtain study sets.

MASSACHUSETTS

State Meeting in Boston.—The 179th annual meeting of the Massachusetts Medical Society will be held May 17-19 at the Statler Hilton Hotel, Boston, under the presidency of Dr. Lawrence R. Dame, Greenfield. The following papers will be presented by out-of-state speakers:

Recent Advances in Aero Space Medicine, Col. John P. Stapp, M.C., U.S.A.F., Dayton, Ohio.
A Method of Clinical Orientation to Alcohol Addition, Dr. R. Gordon Bell, Willowdale, Ont., Canada.
A Dermatologic Clinic, Dr. Walter B. Shelley, Philadelphia.
Curative and Palliative Therapy for Recurrent Cancer of the Cervix, Dr. William W. Daniel, New York City.
Biochemical Basis for Cancer Chemotherapy, Robert W. Brockman, Ph.D., Birmingham, Ala.

The Annual Discourse, "The Role of Diagnostic Roentgenology in the Practice of Medicine," will be given by Dr. Max Ritvo, Boston, the afternoon of May 17, followed by a panel discussion, "Securing Convelescence—Whose Responsibility, the General Practitioner's or the Specialists'?" Dr. Maxwell Finland, Boston, will give the Shattuck Lecture, titled "Treatment of Pneumonia and Other Serious Infections" the morning of May 18. A program of color television presentations and scientific and commercial exhibits are planned. The Honorable Walter H. Judd, M.D., Minneapolis, member of the congressional committee on foreign affairs, will be guest speaker at the banquet May 18, 7 p. m. For information, write Dr. Robert W. Buck, 22 The Fenway, Boston, Secretary.

Seminar on Allergic Disorders.—The second International Seminar on the Treatment of Inhalant Allergic Disorders with Emulsified Extracts will

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Physicians are invited to send to this department items of news of general interest, for example, those relating to society activities, new hospitals, education, and public health. Programs should be received at least three weeks before the date of meeting.

be held at 75 Bay State Road, Boston, during the weekend of May 28 and 29. Members of the American College of Allergists and the American Academy of Allergy are invited to participate. There will be no registration fee. Because of limitations of space, no more than 100 physicians can be accommodated. All participants of the first seminar and the present conjoint study are cordially invited to return and to take an active part in discussing their clinical and laboratory experiences. The Saturday morning sessions will be held from 9 to 10:30 a. m., and from 11 a. m. to 12:30 p. m. The Saturday afternoon session will begin at 2 p. m. and continue until 3:30 p. m., to resume at 4 and last until 6 p. m. There will again be two sessions on Sunday morning and a cocktail party beginning at 3 p. m. on Sunday afternoon and evening. For information, write Dr. Ethan Allan Brown, 75 Bay State Road, Boston 15.

MICHIGAN

Monitor Hearts of Anesthetized Patients.—Every patient given an anesthetic at Grace Hospital, Detroit, has his heart monitored continuously. Fifty heart monitors supplied to the hospital emit "beeping" signals translating the electric-wave activity of a patient's heart. The new devices weigh only 6 oz. each and are less than 5 in. long. Grace Hospital heretofore monitored the heart actions of certain anesthetized patients with larger, bulkier equipment.

Personal.—Dr. Wilson P. Richards, Eloise, was appointed group medical director for seven Chrysler Corporation plants March 19. In his new position Dr. Richards will be responsible for directing activities of medical departments and facilities at the Center Line, Detroit Tank, Highland Park, Marysville, and Michigan Missile plants in the Detroit area, at the Chrysler Airtemp plant in Dayton, Ohio, and at the Missile Division facilities in Huntsville, Ala.——Parke, Davis & Company announced the appointment of Dr. John E. Gajewski, Detroit, as assistant director of medical correspondence and assistant editor of *Therapeutic Notes*, the firm's medical journal.

NEBRASKA

Annual Lecture Given.—Dr. Joseph K. Perloff, director of the Diagnostic Laboratories, Division of Cardiology at Georgetown University Medical Center in Washington, D. C., delivered the annual Phi Rho Sigma Memorial Lecture April 22 at the Creighton University Student Center, Omaha. The lecture honored the late Dr. Adolph Sachs, Omaha physician. Sponsored by the Creighton University chapter of Phi Rho Sigma Medical Fraternity, the lecture was titled "The Physiologic Basis of Heart Sounds and Murmurs."

NEW JERSEY

Biochemist Receives Award.—Milton Gross, Ph.D., director, department of biochemistry, Margaret Hague Maternity Center, Jersey City, received the E. R. Squibb & Sons Prize Paper Award of the American Society for the Study of Sterility. The award winning paper, titled "Cyclic Changes in the Biochemistry of the Female Reproductive Tract," was originally presented at the annual meeting of the Pacific Coast Fertility Society last November and, following a ballot, was judged by the members to be the "best research presentation" at the meeting. The award was made at the 1960 annual meeting of the American Society for the Study of Sterility held recently in Cincinnati.

Meeting of Eye and Ear Specialists.—The New Jersey Academy of Ophthalmology and Otolaryngology in co-sponsorship with the Pennsylvania Academy of Ophthalmology and Otolaryngology will hold a meeting May 19-21 at the Hotel Traymore, Atlantic City, N. J. The program includes the following symposiums:

Medicine and the Public.
Surgery of the Larynx.
Clinical Methods of Examination.
Therapeutic Considerations in Diseases of the Larynx and Lower Airway.
Current Ocular Therapy.

The guest of honor, Dr. William L. Benedict, Rochester, Minn., will present an address May 20. Medical motion pictures and instructional courses are planned. Entertainment includes a golf tournament May 19. For information, write Mr. Randall Norris, 367 New Bridge Rd., Bergenfield, N. J., Executive Secretary.

NEW YORK

Booklet and Films on Hospitalization of Children.—The Parents' Committee of the Children's Ward, Inc., of the Tompkins County Hospital, Ithaca, announced the publication of a booklet, "I Went to the Hospital," and a film, "A New World for Peter," prepared by the organization. The booklet serves to acquaint the preschool child with the hospital experience by presenting the story in "simple but attractive picture form." The film shows children of all ages and their parents what a child's hospitalization is like. Parents' Committee is a volunteer organization whose primary purpose is to assist the hospital in raising and maintaining the standards of its children's ward. For information on the film and booklet, write Mrs. W. R. Sears, Member of Film Committee, Tompkins County Memorial Hospital, Ithaca, N. Y.

New York City

Annual Lecture Given.—The annual Adam M. Miller Memorial Lecture at the State University of New York Downstate Medical Center was delivered on April 25 by Dr. Saul R. Korey, professor of medicine, Albert Einstein College of Medicine. The title of Dr. Korey's talk was "The Glial Cells and Myelinogenesis." The Adam M. Miller Memorial Lecture, established in 1936 by the Theta Chapter of the Phi Lambda Kappa Fraternity in honor of the late Adam M. Miller, professor of anatomy, 1914-1935, and dean of the College of Medicine, 1921-1935, is sponsored by the college.

Conference on Language Disorders in Children.—The second conference on Experimental Classes for Children with Language Disorders (Aphasic Children) will be held at Junior High School 47, 225 E. 23rd St., Friday, May 27, 4 p. m. Helmer R. Myklebust, professor of language pathology and psychology, and director, Institute for Language Disorders, the School of Speech, Northwestern University, Evanston, Ill., will present "Language Disorders in Children—Diagnosis and Training." Chairman of the conference is Dr. William C. Barger, school psychiatrist, Bureau of Child Guidance, Board of Education. General discussion will be sponsored by Parents of Aphasic Children.

Fellowships in Medical Neoplasia.—The Memorial Center for Cancer and Allied Diseases, a training center affiliated with Cornell University Medical College, offers special fellowships for study to a limited number of graduate physicians for the following purposes: (1) to offer the physicians trained in internal medicine the opportunities available at the center to study the natural history, diagnosis, complications, pathogenesis and pathologic physiology, pathology, and treatment of cancer, with particular emphasis on the leukemias, lymphomas, and allied diseases; and (2) to undertake an active supervised clinical investigation of interest to the service and the fellow in the field of medical neoplasia (nonsurgical cancer and palliative therapy of patients with malignant tumors). The fellow will undertake the clinical or clinical and laboratory study of an approved or assigned problem under reasonable guidance and supervision. The study is to be carried out at Memorial Center and under the aegis of the Lymphoma Service of the Department of Medicine. Candidates must be graduates of recognized A. M. A. approved medical schools, and must have completed or be in process of completing two years of postgraduate training in internal medicine in addition to one year of internship. The salary stipend is $6,000 per year without maintenance. The fellowship appointment is for one year, normally beginning July 1, renewable for one or two years. Applicants should apply in writing to Dr. Henry D. Diamond, Chief, Lymphoma Service, Department of Medicine, Memorial Center for Cancer and Allied Diseases, 444 E. 68th St., New York 21.

OHIO

Annual State Meeting in Cleveland.—On May 16-19 the Ohio State Medical Association will hold its 1960 annual meeting, with scientific sessions and exhibits to be held at the Cleveland Public Auditorium, Cleveland. Thirty-seven out-of-state guest speakers are included in the scientific program which includes the following panel discussions:

Precancerous Lesions and Their Treatment.
Cancer Chemotherapy: The Useful Drugs Available and the Indications for Their Use.
Hope for the Cancer Patient with Metastasis.
The Management of Tumors in Childhood.
Coronary Artery Disease—Problems in Management.

The Allen Gerlinger Memorial Lecture, "The Current Status of Thrombolytic Therapy: Its Problems and Future," will be given by Dr. Sol Sherry, St. Louis, the afternoon of May 17. Specialty group meetings and scientific and technical exhibits are planned. The president's ball will be held the evening of May 18. For information, write Mr. C. S. Nelson, 79 E. State St., Columbus 15, Ohio, Executive Secretary.

PENNSYLVANIA

Dr. Dixon to Go to California.—Dr. Frank J. Dixon Jr., chairman, department of pathology, University of Pittsburgh School of Medicine, will become the first director of the new department of experimental pathology, Scripps Clinic and Research Foundation, La Jolla, Calif., July 1, 1961. Also moving to the Scripps from the department of pathology at Pittsburgh are Dr. Joseph D. Feldman, professor of pathology; Dr. Jacinto J. Vazquez, associate professor of pathology; Dr. Gordon B. Pierce, assistant professor of pathology; William O. Weigle, Ph.D., assistant professor of immunochemistry in pathology; and Dr. Charles G. Cochrane, Sarah Mellon Scaife Research Fellow in Pathology and on leave of absence at the Pasteur Institute, Paris. Dr. Dixon, his associates, and their staff will be the first occupants of the new Medical Research Institute of the Scripps Clinic and Research Foundation, which will be completed by July 1, 1961.

Philadelphia

Hospital News.—Lankenau Hospital announced the opening of a department of behavioral sciences within the Division of Research as a further step in its development of a comprehensive research program. Prof. Selden D. Bacon, New Haven, director of Yale University's Center of Alcohol Studies, will serve as head of the new department. During its first year, alcoholism will be the primary research target of the new department.——April 25 marked the official opening of the new $1,150,000 Student Nurses' and Interns' Residence of Pennsylvania Hospital located on the southeast corner of Eighth and Spruce Streets. The four-story brick structure, air-conditioned throughout, has accommodations for 156 in two separate units for student nurses and interns.

University News.—Several faculty members of the Temple University School of Medicine recently were appointed to major local and national offices. They include Dr. Lowrain E. McCrae, president-elect, American Urological Association; Dr. Richard A. Kern, president, Association of Military Surgeons of the United States; Dr. W. Emory Burnett, president, Philadelphia Academy of Surgery; Dr. Harry E. Bacon, president-elect, U. S. Section, International College of Surgeons; Dr. George I. Blumstein, president-elect, American Academy of Allergy.——Three faculty members of the Temple University School of Medicine were appointed advisors to the Professional Section of the Medical Defense Council for the State of Pennsylvania. They are Dr. Kyril B. Conger, head, department of urology; Dr. Chris J. D. Zarafonetis, professor of clinical and research medicine; and Dr. Frederick J. Murtagh Jr., associate professor of neurosurgery.

SOUTH CAROLINA

State Session in Myrtle Beach.—The South Carolina Medical Association will hold its annual scientific session May 18-19 in Myrtle Beach. Dr. William Weston Jr., Charleston, will present the presidential address the afternoon of May 18. A symposium on glaucoma and the following panel discussions are planned: Cardiovascular Diseases, Perinatal Problems, and Hormone and Chemotherapy of Cancer. The following papers will be presented by out-of-state speakers:

Aortic Valvular Disease, Dr. William H. Muller, Charlottesville, Va.
Pregnancy Following Operative Delivery, Dr. Robert A. Cosgrove, Jersey City, N. J.
Obstetrician's Responsibility in the Prevention of Neurologic Disease in Children, Dr. George W. Anderson, Providence, R. I.
Early Management of the Severely Burned Patient, Dr. Edward Krementz, New Orleans.
The Hands in the Diagnosis of Rheumatic Diseases, Dr. Howard L. Holley, Birmingham, Ala.
Natural History of Arteriosclerosis Obliterans, Dr. Edgar V. Allen, Rochester, Minn.
Basis Psychotherapy, Dr. Kenneth E. Appel, Philadelphia.

Scientific and commercial exhibits are planned. For information, write Mr. M. L. Meadows, 309 W. Evans St., Florence, S. C., Executive Secretary.

UTAH

Surgical Meeting in Ogden.—The annual meeting of the Ogden Surgical Society will be held May 18-20 at the Orpheum Theatre, Ogden. A total of 27 papers are scheduled on the program, including "Artificial Mechanical Ventilation and Its Clinical Application" and "Selective Cardioangiography in Congenital and Acquired Heart Disease," by Dr. Clarence Crafoord, Stockholm, Sweden. Participants will include the following: Drs. Alton Ochsner Jr. and Alton Ochsner Sr., New Orleans; Edward H. Hashinger, La Jolla, Calif.; Frank H. Gardner, Boston; Jonathan E. Rhoads, Philadelphia; John P. Caffey, Leonard J. Goldwater, and Heinz F. Eichenwald, New York City; C. Paul Hodgkinson, Detroit; William H. Beierwaltes, Ann Arbor, Mich.; Joel W. Baker, Seattle; A. Edward Maumenee, Baltimore; William H. ReMine, Rochester, Minn.; and Irwin H. Kaiser, Salt Lake City. A panel discussion, "Diseases of the Thyroid," is planned, and discussions on general surgery, internal medicine, pediatrics, and obstetrics-gynecology are scheduled for the afternoon of May 20. For information, write Dr. O. E. Grua, 412 First Security Bank Bldg., Ogden, Utah, Secretary.

WEST VIRGINIA

Dr. Zimmermann Named Surgery Head.—The appointment of Dr. Bernard Zimmermann, of Minneapolis, as head of the West Virginia University Medical Center's department of surgery was announced March 23 by President Elvis J. Stahr Jr. Dr. Zimmermann, professor in the department of surgery, University of Minnesota Medical School, where he has been a member of the staff since 1953, will join the West Virginia faculty full time not later than July 1. He is coordinator of training in cancer at Minnesota. He holds special appointments on the American College of Surgeons Committee on Pre- and Postoperative Care, the U. S. Public Health Service Cancer Chemotherapy Study Section, and the Interim Committee of the Organization of Cancer Coordinators. He is secretary-treasurer of the Minnesota Academy of Medicine.

WISCONSIN

Course on Air Pollution.—A short postgraduate course on the "The Effects of Air Pollution on Environment and Health" will be given by the University of Wisconsin Medical School May 19-20 at the Wisconsin Center. The course is aimed at the interests of physicians, public health personnel, and engineers. It will include discussion of the role of air content in industrial, rural, and home environments in the production of disease. Visiting speakers will include Mr. Ralph J. Van Derwerker, Chicago, regional program director, engineering services, Department of Health, Education, and Welfare; Leonard M. Schuman, professor epidemiology, University of Minnesota College of Medical Sciences; Francis O'Grady, Veterans Administration Hospital, Baltimore; Thomas R. Mazzocco, air pollution medical research, Department of Health, Education, and Welfare, Washington, D. C.; L. Otis Emik, chief, laboratory investigations section, air pollution medical program, Department of Health, Education and Welfare, Washington, D. C.; and

John J. Phair, professor of preventive medicine and industrial health, University of Cincinnati College of Medicine. Registration can be made through Dr. R. C. Parkin, coordinator of graduate medical education, University of Wisconsin Medical School, 418 N. Randall Ave., Madison 6, Wis.

GENERAL

Regional Meeting of Eye and Ear Specialists.—A regional scientific meeting of ophthalmologists and otolaryngologists from six states will be held at the Hotel Traymore, Atlantic City, N. J., May 19-21. Physicians from Pennsylvania, New Jersey, Maryland, Delaware, Virginia, and West Virginia will attend. Any others who wish to attend may secure information from Dr. James E. Landis, 232 N. Sixth St., Reading, Pa. The meeting is sponsored by the Pennsylvania Academy of Ophthalmology and Otolaryngology in conjunction with the New Jersey Academy of Ophthalmology and Otolaryngology.

Plan Daily Medical Newspaper.—The American Research and Development Corporation announced its sponsorship of what is expected to be the first daily medical newspaper published in the United States. The new paper, the *Medical Tribune*, began publication in March as a 32-page edition published on Wednesday. Later in the year the paper will add a Friday edition and, according to current plans, sometime in 1961 will become a daily paper. For information, contact Medical Tribune, Inc., 624 Madison Ave., New York City (Telephone PLaza 1-2814).

Endocrine Meeting in Miami Beach.—The 42nd annual meeting of The Endocrine Society will be held in Eden Roc Hotel, June 9-11. Sessions are planned under the following titles: Adrenal, Pituitary, Reproduction—Calcium Metabolism, Pituitary—Testes, Ovary—Thyroid, Diabetes and Related Metabolism, and Clinical Sessions. At the annual dinner session the evening of June 10, Dwight J. Ingle, Ph.D., will present the president's address following the presentation of awards. A total of 80 papers are listed on the program. For information, write Dr. Harry H. Turner, 1200 N. Walker, Oklahoma City, Executive Secretary.

Medical Unit in South Viet Nam.—Dr. Thomas A. Dooley will soon establish another of his MEDICO teams in South Viet Nam. Dr. Dooley recently returned to Saigon with the idea of bringing in a medical team of the private voluntary training organization. Before continuing to Laos, Dr. Dooley had a meeting with Viet Nam President Nego Dinh Diem, who welcomed the proposal and who decided on the central Viet Nam city of Quang Ngai as the MEDICO team's location. The team will be composed of one American doctor and three or four registered nurses and will work with the same understanding as applies to MEDICO teams elsewhere, that they are there to help the local staff acquire the knowledge and practice to carry on medical treatment effectively long after the Americans leave.

Plastic Surgeons Meeting in Milwaukee.—The annual meeting of the American Association of Plastic Surgeons will be held May 17-20 at the Milwaukee Inn, Milwaukee, under the presidency of Dr. Lyndon A. Peer, East Orange, N. J. Forty-three presentations are scheduled on the program, including two motion pictures, "Evaluation and Treatment of the Congenitally Absent Thumb" and "Surgical Repair of Hypospadias," and the following live clinics: Kidney Transplantation in Identical and Nonidentical Twins, Bilateral Pelvectomy for Paraplegia, and Amputation vs. Reconstruction in Severe Hand Injury. At the annual dinner May 19, 8 p. m., the presentation of the Honorary Award Medal to Dr. Charles C. Guthrie will be followed by an address by the guest speaker, Mr. Rainsford Mowlem, F.R.C.S. A program of ladies' activities is planned. For information, write Dr. Thomas D. Cronin, 6615 Travis St., Houston 25, Texas.

Meeting of Medical Library Group.—The 59th annual meeting of the Medical Library Association, Inc., will be held May 15-20 in Kansas City, Mo., with headquarters at the Muehlebach Hotel. Symposiums are planned under the following titles: "Continuing Education for Medical Librarianship" and "The Society Library in Relation to the Community, Reports on Recent Developments." The following panel discussions are scheduled:

The Supervisor and the Supervised.
From the Clinic into Print to the Physician.
Subject Control of Medical Literature.
Planning a Better Medical School Library.
Psychiatric Literature with a Footnote on Neurology.

Group meetings and luncheons are arranged. Guest speaker at the annual banquet 7:30 p. m., May 19, will be Dr. J. Christian Bay, Librarian Emeritus, The John Crerar Library. Chicago. For information, write Miss Nettie A. Mehne, Upjohn Company Library, 301 Henrietta St., Kalamazoo, Mich., Secretary.

Fellowships for Medical Students.—The Lederle Laboratories Division of the American Cyanamid Company announced that it is making available to medical schools throughout the United States and Canada "Lederle Medical Student Fellowships" for 1960. These fellowships, in amounts not exceeding $600 per year for any individual, are "intended to relieve in part the financial burden of students who desire to devote their summer vacations to research in the preclinical departments." Students who apply for the research fellowships must be of "good scholastic standing" and must have the consent of the faculty member under whose supervision their research is to be conducted. The selection of students to receive such awards will be made by the dean of the medical school, or by the regularly constituted committee of the faculty charged with such selections. By special permission of the dean or the fellowship committee of the school, the student may carry on such research in another medical school provided that satisfactory arrangements are previously made with the faculty member of the school and the department in which the student is to carry on his research.

Plan Putting Diabetes Data on Tape.—A group of experts from throughout the country is working to bring together, on magnetic tape, the world's writings on diabetes and subjects related to the disease. Dr. Joseph L. Izzo, Rochester, N. Y., will serve as editor of the *Diabetes Abstract*, envisaged by the group as a regularly published journal containing abstracts of up-to-date information on diabetes from all over the world. When all the data on diabetes is collected (expected to take a few years) it will be abstracted and stored on magnetic tapes in a machine specifically designed for the undertaking by General Electric Company. A specialist will then be able to refer to the center for all the available information on a certain aspect of diabetes. A committee has been established under a grant from the National Institutes of Health to do the job. The chairman is Dr. Arnold Lazarow, chairman, department of anatomy, University of Minnesota School of Medicine, Minneapolis. Where the center will be has not yet been decided. One roll of tape can contain 1,000 to 1,200 articles. With the new machine, an entire tape can be screened for a particular subject in 21 minutes. Fifteen separate screenings can be made simultaneously.

Establish Council for Science Writing.—The establishment of a Council for the Advancement of Science Writing (CASW) was announced Feb. 21. Its purpose is "to stimulate an increase in the quantity and quality of science news that is carried in all media of mass communications—newspapers, television, radio, magazines, and books for the general public." It plans to do this by fostering research and training in science journalism and by sponsoring discussions and seminars on science writing throughout the country. The council, a nonprofit corporation registered in the state of New York, was launched through the efforts of the National Association of Science Writers. Those elected to the CASW at its first meeting in New York City included Mr. Pierre C. Fraley, president, National Association of Science Writers, and Dr. H. Jack Geiger, Pickville, Ky. The idea for an organization such as the Council for the Advancement of Science Writing came out of a conference held by the National Association of Science Writers in New York several years ago. Pending the opening of an office of its own, the CASW may be reached through the Secretary, Prof. Hillier Krieghbaum, Department of Journalism, New York University, New York City.

Organize International Workshop in Neurology.—The first meeting of the Workshop for Comparative Neurology and Neuropathology was held Nov. 28-29, 1959, at the Veterinary Medical Faculty, University of Berne, Switzerland. The meeting was held under the chairmanship of Dr. L. von Bogaert, of the Institute Bunge, of Antwerp, president, World Federation of Neurology. The group will concern itself with the two disciplines, comparative neurology and neuropathology, for the following purposes: to arrange conventions, participate in congresses, symposiums, and seminars, and promote research in neurology and neuropathology for the benefit of clinical neurology. The secretariat of the organization plans to promote the exchange of technical reports, publications, and research material. The group will classify and index existing special collections, preserve them, and make them generally available. It will compile a list of those interested in comparative neuropathology and will encourage them to participate in the research of the workshop. All communications should be addressed to the secretary, Prof. Dr. E. Frauchiger, Veterinary-Ambulatory Clinic, University of Bern, Neubruckstrasse 10, Switzerland.

Annual Meeting of Orthopedists.—The 73rd annual session of the American Orthopaedic Association will be held May 30-June 2 at the Homestead, Hot Springs, Va. Guest of Honor will be Dr. Henry L. Jaffe, New York City, who will present "Diagnostic Problems Raised by Myositis Ossificans and Certain Other Lesions" the morning of May 31. The following papers will include invited authors:

Eosinophilic Granuloma 'One of Three Sisters,' Dr. Charles A. Rockwood Jr., Oklahoma City.
Sarcoma in Paget's Disease of Bone, Dr. Hugh C. Barry, Sydney, Australia.
Prognosis in Fractures of the Acetabulum, Dr. J. Drennan Lowell, Boston.
Complete Dislocation and Subluxation of the Acromioclavicular Joint: End Result in 70 Cases, Drs. Patrick J. Kelly, Rochester, Minn., Marco A. Lazcano, Mexico City, and Sanford A. Anzel, Shaw Air Force Base, S. C.
Anterior Chamber Angle of the Eye in Patients with Idiopathic Scoliosis, Drs. Gunter K. Von Noorden, and Herman M. Burian, Iowa City.
Surgical Instrumentation for Management of Scoliosis, Dr. Paul R. Harrington, Houston.
Hip Pathology in the Patient with Cerebral Palsy, Dr. Richard A. Dodelin, Durham, N. C.

Dr. John R. Moore, Philadelphia, will present the presidential address the morning of June 1, and at the annual banquet that evening Col. John P. Stapp, M. C., U. S. A. F., of the Aeromedical Space Laboratory, Wright Patterson Air Force Base, Ohio, will be guest of honor. For information, write Dr. Lee R. Straub, 535 E. 70th St., New York 21, Secretary.

Markle Scholarships.—Twenty-five medical scientists, faculty members of medical schools in the United States and Canada, were appointed Markle Scholars in Medical Science by the John and Mary R. Markle Foundation of New York. Each appointment carries with it a $30,000 grant, paid to the medical school where the scholar will teach and do research at the rate of $6,000 a year and used to supplement the scholar's support and to aid his research for the next five years. The scholars whose appointments began in 1960, their fields of interest, and the medical schools that will receive grants toward their support are:

Dr. Gonzalo Enrique Aponte, pathology, Jefferson Medical College of Philadelphia.
Dr. J. Thomas August, internal medicine, Stanford University School of Medicine, Palo Alto, Calif.
Dr. Dana C. Brooks, anatomy, Cornell University Medical College, New York.
Dr. Lamar E. Crevasse, Jr., internal medicine, University of Florida College of Medicine, Gainesville.
Dr. John Robert Evans, internal medicine, University of Toronto Faculty of Medicine, Toronto, Ont.
Dr. James J. Ferguson Jr., internal medicine, University of Pennsylvania School of Medicine, Philadelphia.
Dr. Robert A. Fishman, neurology, Columbia University College of Physicians and Surgeons, New York.
Dr. John R. G. Gosling, obstetrics and gynecology, University of Michigan Medical School, Ann Arbor.
Dr. Joseph A. Hinke, anatomy, University of British Columbia Faculty of Medicine, Vancouver.
Dr. Charles H. Hollenberg, internal medicine, McGill University Faculty of Medicine, Montreal, Que.
Dr. William D. Huffines, pathology, University of North Carolina School of Medicine, Chapel Hill.
Dr. Frank L. Iber, internal medicine, Johns Hopkins University School of Medicine, Baltimore.
Dr. Stanley W. Jacob, surgery, University of Oregon Medical School, Portland.
Dr. Richard C. Lillehei, surgery, University of Minnesota Medical School, Minneapolis.
Dr. James F. Lind, surgery, University of Manitoba Faculty of Medicine, Winnipeg.
Dr. John C. Loesch, psychiatry, University of Illinois College of Medicine, Chicago.
Dr. Frank I. Marcus, internal medicine, Georgetown University School of Medicine, Washington, D. C.
David S. Maxwell, Ph.D., anatomy, University of California at Los Angeles School of Medicine.
Dr. Richard L. Naeye, pathology, University of Vermont College of Medicine, Burlington.
Dr. Hubert C. Pirkle, pathology, University of Louisville (Ky.) School of Medicine.
Dr. Frank R. Schmid, internal medicine, Northwestern University Medical School, Chicago.
Dr. Seymour I. Schwartz, surgery, University of Rochester (N. Y.) School of Medicine and Dentistry.
Dr. Daniel B. Stone, internal medicine, State University of Iowa College of Medicine, Iowa City.
Dr. Ralph J. Wedgwood, pediatrics, Western Reserve University School of Medicine, Cleveland.
Dr. G. Rainey Williams, surgery, University of Oklahoma School of Medicine, Oklahoma City.

FOREIGN

Audiology Congress in Bonn.—The fifth congress of the International Society of Audiology will be held Sept. 28-Oct. 2 in Bonn, Germany, at the University Ear-Nose-and-Throat Clinic. The theme for the program will be "Differential Diagnosis of Aural Disorders," for which three round-table discussions are planned as follows: (1) Central and Cortical Deafness with Adults; (2) Physiology, Functional Pathology and the Clinical Significance of "Recruitment"; (3) Adaptation and Aural Fatigue, Associated Symptoms and Their Clinical Significance. The official languages of the congress will be German, English, French, and Spanish, and simultaneous translation and recording services will be available. For information, write the Congress Office, Universitäts-Hals-Nasen-Ohrenklinik, Bonn-Venusberg, Germany.

Emphasis on Preventive Medicine in Western Nigeria.—Western Nigeria plans to switch its health program from hospital construction to preventive medicine during the next five years. The chief aim of the new program, according to J. Ola Adigun, minister of health and social welfare, is to "reduce the incidence of disease and to cut down the need for treatment in medical institutions." Mr. Adigun pointed out that the preventive medical scheme is part of the Western Region's Five Year Development Plan which entails a total expenditure of $462 million. In conjunction with its new health education program, Western Nigeria also plans to encourage the establishment of private medical institutions. To do this it has allocated over $3 million to meet the capital costs of hospitals and medical centers that can be operated on a sound basis by private concerns or individuals.

Socialization of Physicians Under Communism.—An article appearing in *Frankfurter Allgemeine Zeitung* and reprinted in the January *Bayerisches Aerzteblatt* reports that in November, 1959, a Bucharest court sentenced a physician in Fetesti to five years of "corrective imprisonment" because it was proved that he accepted fees from private patients. Shortly before, a Czechoslovakian physician in Prague was sentenced to pay a fine of three months' salary because of the same "offense." Another physician, who, "in spite of the explicit prohibition of the Health Office, continued treating private patients," was sentenced to 18 months in jail. In October, 1959, Radio Moscow announced a resolution by a group of Soviet physicians in Rostow: "There shall not be a private practice in our life any longer; this reminder of the past must disappear." The *Bayerisches Aerzteblatt* stated that the development of socialization of the health service has progressed farthest in Rumania and Czechoslovakia. In Hungary 50% of the physicians were forced to give up their private practices. In Poland, however, the socialization is delayed because of social and economic difficulties. It was reported that 3,300 physicians fled to West Germany from East Germany from 1954 to August, 1959.

CORRECTION

Local Injection Therapy for Rheumatic Diseases.—An error appeared in the contribution by Drs. Finder and Post entitled "Local Injection Therapy for Rheumatic Diseases," in THE JOURNAL, April 30, page 2021. The first sentence after the side-head *Choice of Drug*, on page 2024, should read, "Equally competent reporters were in disagreement about the comparative duration of effect of hydrocortisone tertiary butylacetate (TBA) and prednisolone TBA."

EXAMINATIONS AND LICENSURE

EDUCATIONAL COUNCIL FOR FOREIGN MEDICAL GRADUATES, INC.

Educational Council for Foreign Medical Graduates: Stations around the world. Sept. 21, 1960. Exec. Director, Dr. Dean F. Smiley, 1710 Orrington Ave., Evanston, Ill.

NATIONAL BOARD OF MEDICAL EXAMINERS

National Board of Medical Examiners: Part I, Various Cities, June 21-22 and Sept. 7-8. Part II. Applications must be received at least six weeks before the date of the examination. Exec. Sec., Dr. John P. Hubbard, 133 South 36th St., Philadelphia.

BOARDS OF MEDICAL EXAMINERS

ALABAMA: *Examination.* Montgomery, June 21-23. Sec., Dr. D. G. Gill, State Office Bldg., Montgomery.

ALASKA:* On application in Anchorage or Fairbanks. Sec., Dr. W. M. Whitehead, 172 South Franklin St., Juneau.

ARKANSAS:* *Examination and Reciprocity.* Little Rock, June 9-10 Sec., Dr. Joe Verser, Harrisburg.

CALIFORNIA: *Written.* San Francisco, June 20-23; Los Angeles, Aug. 22-25 and Sacramento, Oct. 17-20. *Oral and Clinical.* Los Angeles, San Francisco, June 19; Los Angeles, Aug. 21, and Los Angeles, Nov. 29. *Oral for Reciprocity Applicants.* San Francisco, June 18; Los Angeles, Aug. 20 and Nov. 19. Sec., Dr. Louis E. Jones, Room 536, 1020 N Street, Sacramento.

CANAL ZONE: On Application. Acting Sec., Dr. B. K. Levin, Health Bureau, Balboa Heights.

COLORADO:* *Examination.* Denver, June 14-15. Sec., Dr. John B. Farley, 1612 Tremont Place, Denver 2.

CONNECTICUT:* Hartford, July 13-14. Sec., Dr. Stanley B. Weld, 160 St. Ronan St., New Haven.

DELAWARE: *Examination and Endorsement.* Dover, June 12-14 and July 21. Sec., Dr. Joseph S. McDaniel, Professional Bldg., Dover.

DISTRICT OF COLUMBIA:* *Examination.* Washington, June 13-14. Deputy Director, Mr. Paul Foley, Department of Occupations and Professions, 1740 Massachusetts Ave., N.W., Washington 6.

FLORIDA:* *Examination.* Miami Beach, June 19-21. Sec., Dr. Homer L. Pearson, 901 N.W. 17th St., Miami 36.

GEORGIA: *Examination.* Atlanta and Augusta, June 8-9. *Reciprocity.* Atlanta and Augusta, June 10. Sec., Mr. Cecil L. Clifton, 224 State Capitol, Atlanta 3.

GUAM: *Subject to Call.* Act Sec., Dr. F. L. Conklin, Agana.

IDAHO: *Examination and Endorsement.* Boise, July 11-13. Exec. Sec., Mr. Armand L. Bird, 358 Sonna Bldg., Boise.

INDIANA: *Examination.* Indianapolis, June 22-24. *Reciprocity.* Indianapolis, fourth Wednesday of each month. Ex. Sec., Miss Ruth V. Kirk, 538 K. of P. Bldg., Indianapolis.

ILLINOIS: *Examination.* Chicago, July 12-14. *Reciprocity.* Chicago, July 15. Supt. of Registration, Mr. Frederic B. Selcke, Capitol Bldg., Springfield.

KANSAS:* *Examination.* Kansas City, June 16-17. *Endorsement.* Kansas City, June 18. Sec., Dr. F. J. Nash, New Brotherhood Bldg., Kansas City.

KENTUCKY: *Examination.* Louisville, June 6-7. Sec., Dr. Russell E. Teague, 620 South Third St., Louisville 2.

LOUISIANA: *Examination and Reciprocity.* New Orleans, June 9-11. Sec., Dr. Edwin H. Lawson, 930 Hibernia Bank Bldg., New Orleans 12. *Homeopathic.* Examination subject to call. Sec., Dr. F. H. Hardenstein, 903 Pere Marquette Bldg., New Orleans.

MARYLAND: *Examination.* Baltimore, June 15-18. Sec., Dr. Frank K. Morris, 1215 Cathedral St., Baltimore 1.

MASSACHUSETTS: *Examination.* Boston, July 12-15. Sec., Dr. David W. Wallwork, Room 37, State House, Boston 33.

MICHIGAN:* *Examination.* Ann Arbor and Detroit, June 6-8. Sec., Dr. E. C. Swanson, 118 Stevens T Mason Bldg., Lansing.

MISSISSIPPI: *Examination.* Jackson, June 20-21; *Reciprocity,* Jackson, June 16. Sec., Dr. A. L. Gray, Old Capitol, Jackson 13.

MISSOURI: *Examination.* St. Louis, May 27-28. Exec. Sec., Mr. John A. Hailey, State Capitol Bldg., P. O. Box 4, Jefferson City.

MONTANA: *Examination and Reciprocity.* Helena, Oct. 4. Sec., Dr. Thomas L. Hawkins, 555 Fuller Ave., Helena.

NEBRASKA:* *Examination.* Omaha, June 13-15, 1960. Dir., Bureau of Examining Boards, Room 1009, State Capitol Bldg., Lincoln 9.

NEVADA: *Examination and Reciprocity.* Reno, June 8, Sept. 7 and Dec. 7. Sec., Dr. G. H. Ross, 112 North Curry St., Carson City.

NEW HAMPSHIRE: *Examination and Reciprocity.* Concord, Sept. 14-17. Sec., Dr. Edward W. Colby, 61 South Spring St., Concord.

NEW JERSEY: *Examination.* Trenton, June 21-24. *Reciprocity.* Continuously. Sec., Dr. Royal A. Schaaf, 28 West State St., Trenton.

NEW YORK: *Examination.* Albany, Buffalo, New York City, Rochester and Syracuse, June 28-July 1. Sec., Dr. Stiles D. Ezell, 23 S. Pearl Street, Albany.

NORTH CAROLINA: *Examination and Endorsement.* Raleigh, June 20-23. Sec., Dr. Joseph J. Combs, 716 Professional Bldg., Raleigh.

NORTH DAKOTA: *Examination and Reciprocity.* Grand Forks, July 13-16. Sec., Dr. C. J. Glaspel, Grafton.

OHIO: *Reciprocity.* Columbus, June 17. *Examination.* Columbus, June 16-18. Sec., Dr. H. M. Platter, 21 West Broad St., Columbus 15.

OKLAHOMA:* *Examination and Endorsement.* Oklahoma City, May 31-June 1. Sec., Dr. E. F. Lester, 813 Braniff Bldg., Oklahoma City.

OREGON:* *Examination.* Portland, July. Exec. Sec., Mr. Howard I. Bobbitt, 609 Failing Bldg., Portland.

PENNSYLVANIA: *Examination.* Philadelphia and Pittsburgh, July 5-7. Sec., Mrs. Margaret G. Steiner, Box 911, Harrisburg.

DEATHS

Abbey, Frank Lincoln, Newton, Kan.; Washington University School of Medicine, St. Louis, 1924; died March 9, aged 63.

Baxter, Albert Crum Ⓜ Springfield, Ill.; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1907; served as director of the state department of public health, health superintendent of Springfield, chairman of the county board of supervisors, and health officer of Decatur; died in the Memorial Hospital March 17, aged 79, of coronary thrombosis.

Benson, Oscar Theodore Ⓜ Los Angeles; University of Minnesota College of Medicine and Surgery, Minneapolis, 1905; for many years practiced in Glen Ullen, N. D., where he was president of the school board for many years; died March 7, aged 80.

Bigelow, Charles Tate Ⓜ St. Petersburg, Fla.; Baltimore Medical College, 1897; formerly practiced in Oxford, Iowa, and Clinton, Iowa; died March 9, aged 82.

Binkley, Owen Henry Ⓜ Hagerstown, Md.; Jefferson Medical College of Philadelphia, 1917; veteran of World War I; died in the Veterans Administration Hospital, Perry Point, March 12, aged 66.

Bird, Arthur Judson Ⓜ New Albany, Pa.; University of the South Medical Department, Sewanee, Tenn., 1895; for many years practiced in Overton; veteran of World War I; died in the Robert Packer Hospital, Sayre, March 8, aged 88.

Bogen, Esther Ⓜ Los Angeles; born in Woodbine, N. J., March 6, 1901; University of Cincinnati College of Medicine, 1927, and received a Ph.D. in 1935; specialist certified by the American Board of Psychiatry and Neurology; member of the American Psychiatric Association and the Association for Research in Nervous and Mental Diseases; certified by the National Board of Medical Examiners; associate clinical professor of psychiatry at the College of Medical Evangelists, Loma Linda and Los Angeles; formerly associated with the women's psychiatric division, Longview State Hospital in Cincinnati; on the staff of the Los Angeles County Hospital; joint author of "Art and Science of Marriage"; died in Pasadena March 14, aged 58.

Brown, Marshall Stewart Jr., Sarasota, Fla.; University and Bellevue Hospital Medical College, New York City, 1929; formerly practiced in New York City, where he was associated with the Bellevue and Lenox Hill hospitals; veteran of World War II and received the French Croix de Guerre; died March 20, aged 56.

Bryan, Charles Edward, Riverside, R. I.; Hahnemann Medical College and Hospital of Philadelphia, 1942; interned at the Homeopathic Hospital in Providence; member of the American Academy of General Practice and past-president of the Rhode Island Academy of General Practice; veteran of World War II; served as police surgeon for the East Providence Police Department; a staff member and secretary of the medical staff of the Roger Williams General Hospital, Providence, where he died March 9, aged 44.

Charache, Herman Ⓜ Brooklyn; New York Homeopathic Medical College and Flower Hospital in New York City, 1929; associated with the Cumberland Hospital, Jewish Chronic Disease Hospital, and the Prospect Heights Hospital, where he died March 20, aged 63.

Coburn, Harry Ray Ⓜ Bryantown, Md.; Tufts College Medical School, Boston, 1908; served on the staff of the Tewksbury (Mass.) State Hospital; died March 18, aged 77.

Conduff, Charles Edward Ⓜ Roanoke, Va.; Tennessee Medical College, Knoxville, 1908; died in the Shenandoah Hospital Jan. 27, aged 76, of peritonitis following perforation of gangrenous gallbladder.

Conover, Charles Higbee, Pleasantville, N. J.; Hahnemann Medical College and Hospital of Philadelphia, 1899; veteran of World War I; served as president of the board of education; associated with the Shore Memorial Hospital in Somers Point; died in the Hahnemann Hospital, Philadelphia, March 7, aged 86.

Cosgrove, Samuel Allison Ⓜ Jersey City, N. J.; born in 1883; Cornell University Medical College, New York City, 1907; specialist certified by the American Board of Obstetrics and Gynecology; member of the American Association of Obstetricians and Gynecologists and the American Gynecological Society; fellow of the International College of Surgeons and the American College of Surgeons and served on its board of governors; veteran of World War I; formerly member and president of the state board of health; served on the faculty of Seton Hall College of Medicine and Dentistry in Jersey City and the Columbia University College of Physicians

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Ⓜ Indicates Member of the American Medical Association.

and Surgeons in New York City; associated with the Nassau Hospital in Mineola, N. Y., Mountainside Hospital, Montclair, Monmouth Memorial Hospital in Long Branch, Holy Name Hospital in Teaneck, North Hudson Hospital in Weehawken, Bayonne (N. J.) Hospital, and the Christ Hospital and Margaret Hague Maternity Hospital, where he was at one time medical director and superintendent; died Feb. 28, aged 76, of cerebrovascular accident.

Crockett, Melvin Butcher, Tazewell, Va.; University College of Medicine, Richmond, 1895; during World War I and World War II served on the Selective Service examining board; an honorary staff member of Bluefield (W. Va.) Sanitarium; died March 10, aged 87.

Crounse, David Ryerson Ⓜ Passaic, N. J.; Columbia University College of Physicians and Surgeons. New York City, 1895; associated with the Passaic General Hospital and St. Mary's Hospital; died March 10, aged 92.

Dabbs, John Taylor, Nettleton, Miss.; Atlanta College of Physicians and Surgeons, 1906; died Feb. 8, aged 83.

De Baun, Ralph, Congers, N. Y.; Columbia University College of Physicians and Surgeons, New York City, 1903; served as Clarkstown health officer for many years; formerly physician at the Rockland County Jail in New City and school physician in Congers and New City; died March 20, aged 79.

Dixon, George Lane Ⓜ Tucson, Ariz.; born in Burlington, Iowa, July 13, 1895; State University of Iowa College of Medicine, Iowa City, 1922; specialist certified by the American Board of Orthopaedic Surgery; member of the American Fracture Association, American Academy of Orthopaedic Surgeons, and the American Rheumatism Association; past-president of the Pima County Medical Society; fellow of the American College of Surgeons; veteran of World War I and received the Croix de Guerre from the French government; at one time taught at the University of Southern California School of Medicine in Los Angeles, and served on the staff of the Los Angeles County Hospital; associated with the Tucson Medical Center, Veterans Administration Hospital, and St. Mary's Hospital, where he died March 7, aged 64.

Dorsey, Charles Fleming Ⓜ Brookhaven, Miss.; Tulane University School of Medicine, New Orleans, 1939; interned at the Baroness Erlanger Hospital in Chattanooga, Tenn., and served a residency at the Matty Hersee Hospital in Meridian, Miss.; veteran of World War II; died in the King's Daughters Hospital Feb. 27, aged 44.

Dysart, William Patton, Columbia, Mo.; Missouri Medical College, St. Louis, 1887; veteran of World War I; on the staff of Boone County Hospital, where he died March 10, aged 94, of acute pneumonitis.

Edwards, Glenn Graham, Willard, Ohio; Starling–Ohio Medical College, Columbus, 1909; served on the staff of the Gallipolis (Ohio) State Institute; at one time member of the board of education; formerly an examiner for the Baltimore and Ohio Railroad; died in the Willard Municipal Hospital March 12, aged 76.

Eyster, John Augustus English Ⓜ Fort Myers, Fla.; Johns Hopkins University School of Medicine, Baltimore, 1905; member of the Association of American Physicians; fellow of the American College of Physicians; served as professor of physiology at the University of Wisconsin Medical School in Madison, on the faculty of his alma mater and the University of Virginia School of Medicine in Charlottesville; veteran of World War I; for a time consulting physiologist in the U. S. Bureau of Mines; author of "Clinical Aspects of Venous Pressure"; died March 5, aged 78.

Fite, Ped La Fayette, Columbus, Miss.; Memphis (Tenn.) Hospital Medical College, 1901; formerly practiced in Byhalia, where he was founder and first president of the Bank of Byhalia; died March 9, aged 79.

Gilbert, Kramer Martin Ⓜ Chandler, Ariz.; Drake University College of Medicine, Des Moines, Iowa, 1908; past-president of the Chandler Chamber of Commerce; died in Mesa March 6, aged 78.

Goyette, Sidney Aloysius, Nicolaus, Calif.; Eclectic Medical College, Cincinnati, 1913; died in the John C. Fremont Hospital in Mariposa Feb. 11, aged 78.

Grubbe, Emil Herman Ⓜ Chicago; the Hahnemann Medical College and Hospital, Chicago, 1898; specialist certified by the American Board of Radiology; last February, the American Cancer Society bestowed its national citation for distinguished service upon him; underwent 93 operations for radiation burns; died in the Swedish Covenant Hospital March 85, of cancer of the lungs.

Hansen, Anthony Hans Ⓜ Douglaston, N. Y.; Cornell University Medical College, New York City, 1903; died in the North Shore Hospital Feb. 17, aged 81.

Hausherr, Walter Carl, Staten Island, N. Y.; born in Dixon, Ill., March 17, 1894; University of Pennsylvania School of Medicine, Philadelphia, 1918; specialist certified by the American Board of Preventive Medicine; member of the Association of Life

Insurance Medical Directors of America; fellow of the American College of Physicians; from 1919 to 1928 directed field studies in public health and research for the Rockefeller Foundation in the British West Indies, South America, and the southern United States; veteran of World War I; in 1929 joined the Prudential Insurance Company's home office in Newark, N. J., as medical supervisor, became assistant medical director in 1937, and associate medical director and director of the company's laboratory in 1943, retiring in 1959; associated with St. Vincent's and Sea View hospitals; died Feb. 25, aged 65, of cerebral hemorrhage.

Hinchliffe, Frederick, Cohasset, Mass.; Tufts College Medical School, Boston, 1905; past-president of the Norfolk South District Medical Society; veteran of World War I; served as a member of the board of health, a director and president of the Pratt Memorial Library, and physician for the Cohasset schools; died March 9, aged 83.

Hull, Walter Samuel Ⓜ St. Joseph Mo.; University Medical College of Kansas City, 1900; served as county health officer; died March 8, aged 86.

Kaizler, Irene Mayer, Topeka, Kan.; Magyar Kiralyi Pazmany Petrus Tudomanyegyetem Orvosi Fakultasa, Budapest, Hungary, 1950; interned at the Johnston-Willis Hospital in Richmond, where he served a residency; served a residency at the Topeka State Hospital; died March 4, aged 33.

Karl, William Crane Ⓜ Williston Park, N. Y.; Albany, (N. Y.) Medical College, 1938; interned at St. Vincent's Hospital in New York City and the Nathan Littauer Hospital in Gloversville; served a residency at St. Vincent's Hospital in New York City; certified by the National Board of Medical Examiners; veteran of World War II; died March 9, aged 48.

Kelley, John Edward, Chicago; Northwestern University Medical School, Chicago, 1905; on the staff of the Mercy Hospital, where he died March 19, aged 77, of bronchopneumonia.

MacCracken, William Benjamin, Huntington, W. Va.; born in Mount Vernon, N. Y., Sept. 2, 1907; Columbia University College of Physicians and Surgeons, New York City, 1932; interned at the Bellevue Hospital in New York City, where he served a residency; served a residency at the New York Orthopaedic Dispensary and Hospital in New York City, where he also served a fellowship; certified by the National Board of Medical Examiners; specialist certified by the American Board of Orthopaedic Surgery; member of the Southeastern Surgical Congress and the American Academy of Orthopaedic Surgeons; fellow of the International College of Surgeons; veteran of World War II and was awarded the Navy Cross; associated with the Cabell Huntington Hospital, Chesapeake and Ohio Hospital, St. Mary's Hospital, and the Rowley Clinic Hospital; died Feb. 29, aged 52.

Pullen, Roscoe Le Roy, Spokane, Wash.; born in Princeville, Ill., Jan. 6, 1915; Northwestern University Medical School, Chicago, 1940; specialist certified by the American Board of Internal Medicine; fellow of the American College of Physicians; served as dean and professor of medicine at the University of Missouri School of Medicine in Columbia, professor of clinical medicine at Baylor University College of Medicine in Houston, director of graduate medicine and vice-dean at Tulane University of Louisiana School of Medicine in New Orleans, dean and professor of medicine at the University of Texas Postgraduate School of Medicine in Houston, and associate professor of medicine and director of hospital planning at the University of Washington in Seattle; consultant to the surgeon general, U. S. Army, from 1947 to 1953; served as director of University Hospitals in Columbia, Mo., and medical consultant and executive officer of the Missouri State Crippled Children's Program; in 1945 was chosen by Knox College, Galesburg, Ill., as recipient of the award for the alumnus who did the most for humanity during the year; died March 5, aged 45, of coronary thrombosis.

Quinn, Francis Michael, Minersville, Pa.; Hahnemann Medical College and Hospital of Philadelphia, 1912; veteran of World War I; served as president of the board of health; on the staff of the Lemos B. Warne Hospital and Clinic in Pottsville; died in the Jefferson Hospital, Philadelphia, March 7, aged 70.

Riess, Carl John Ⓜ Pontiac, Ill.; University of Colorado School of Medicine, Denver, 1927; died Feb. 29, aged 62.

Riser, Luther Allen Ⓜ Columbia, S. C.; University of Maryland School of Medicine, Baltimore, 1908; for many years head of the county health department of the state board of health; in 1945 resigned as director of the department of vital statistics of the state board of health; retired from the Veterans Administration March 31, 1956; at one time associated with the Pilot Life Insurance Company in Greensboro, N. C.; died in the Columbia Hospital Feb. 29, aged 82.

Rosenthal, Samuel D., Chicago; Chicago College of Medicine and Surgery, 1913; for many years medical director for Goldblatt's stores; on the staff of the Franklin Boulevard Community Hospital; died in the Albert Merritt Billings Hospital March 16, aged 69, of cancer of the pancreas.

Russell, Charles Richard, Lenoir, N. C.; University College of Medicine, Richmond, 1909; died Feb. 29, aged 76.

Sayre, Frank Merrick Ⓜ Canton, Ohio; Starling-Ohio Medical College, Columbus, 1911; for many years associated with the city health department, serving as health commissioner for 22 years; veteran of World War I; died March 1, aged 71.

Schofield, Elmer Clarke Ⓜ Orange, Texas; University of Louisville (Ky.) School of Medicine, 1930; served in the regular Army; on the staff of the Orange Memorial Hospital; died March 3, aged 60.

Schwarz, Leopold Ⓜ Wildwood, N. J.; Schlesische-Friedrich Wilhelms Universität Medizinische Fakultät, Breslau, Prussia, Germany, 1915; died in the Jackson Memorial Hospital, Miami, Fla., Jan. 28, aged 75, of massive cerebral infarction and cerebral arteriosclerosis.

Sendker, Raymond William Ⓜ Buffalo, N. Y.; University of Buffalo School of Medicine, 1924; veteran of World War I; died in St. Petersburg, Fla., March 1, aged 60.

Shadman, Alonzo Jay, Forest Hills, Mass.; Boston University School of Medicine, 1905; died March 6, aged 82, of heart disease.

Sherlock, John Hodges, Stockton, Calif.; Indiana Medical College, School of Medicine of Purdue University, Indianapolis, 1906; died Feb. 28, aged 81.

Smith, Marcus Taylor, Tichnor, Ark.; University of Tennessee Medical Department, Nashville, 1900; died March 2, aged 85.

Stewart, Harrison Morton Ⓜ Holden, Mass.; College of Physicians and Surgeons, Baltimore, 1915; veteran of World Wars I and II; served as medical consultant to the insurance division of the Veterans Administration in Washington, D. C.; died March 7, aged 71.

Sutherland, Harry Nicholas, Ely, Minn.; Rush Medical College, Chicago, 1912; served as health officer of Ely for many years; died Feb. 28, aged 75.

Sweeny, Joseph Bernard Ⓜ Spokane, Wash.; Marquette University School of Medicine, Milwaukee, 1942; interned at the San Francisco Hospital in San Francisco, where he served a residency at St. Mary's Hospital; veteran of World War II; on the staff of Sacred Heart Hospital; died March 4, aged 46.

Sybenga, Jacob John, Pella, Iowa; Northwestern University Medical School, Chicago, 1911; fellow of the American College of Surgeons; veteran of World War I; died March 3, aged 73.

Templeton, Clinton Monroe Ⓜ Augusta, Ga.; University of Georgia Medical Department, Augusta, 1937; interned at the University Hospital in Augusta, where he served a residency; member of the American Academy of General Practice; past-president of the Richmond County Medical Society; veteran of World War II; died near McCormick, S. C., Feb. 28, aged 45.

Turgeon, Leo Victor Ⓜ Topeka, Kan.; University Medical College of Kansas City, Mo., 1913; for many years secretary of the Central Kansas Medical Society, of which he was past-president; served as a member of the state board of administration; died March 5, aged 69.

Warrick, Luby Albert Ⓜ Goldsboro, N. C.; George Washington University School of Medicine, Washington, D. C., 1923; died March 1, aged 60.

Whimster, William Caven, Kansas City, Kan.; Hospital College of Medicine, Louisville, 1898; also a druggist; died March 9, aged 85.

White, George Douglas, Jersey City, N. J.; Columbia University College of Physicians and Surgeons, New York City, 1902; chief chemist for Jersey City for many years and was Jersey City plant physician for Mutual Chemical Company of America; died March 6, aged 81.

Wiant, Herman Ernest Ⓜ Haddonfield, N. J.; Jefferson Medical College of Philadelphia, 1931; interned at the Cooper Hospital in Camden; died March 14, aged 61.

Willner, Victor Ⓜ Woodmere, N. Y.; Universite de Paris Faculte de Medecine, France, 1935; specialist certified by the American Board of Internal Medicine; member of the American College of Gastroenterology; an associate, American College of Physicians; veteran of World War II; on the staffs of St. Joseph's Hospital in Far Rockaway, Mount Sinai Hospital, New York City, Meadowbrook Hospital in Hempstead, and Long Island Jewish Hospital in New Hyde Park; died March 12, aged 51.

Wilson, John Stewart Ⓜ New Bethlehem, Pa.; Temple University School of Medicine, Philadelphia, 1932; veteran of World War II; died March 1, aged 55.

Wyatt, Randall Everett, Nashville, Tenn.; University of Tennessee College of Medicine, Memphis, 1913; also a pharmacist; formerly on the faculty of Vanderbilt University School of Medicine; veteran of World War I; for many years a member and at one time vice-president of the county board of health; associated with the Nashville General Hospital and the Baptist Hospital, where he died Feb. 29, aged 68, of pulmonary emphysema and insufficiency.

FOREIGN LETTERS

FRANCE

Trihydroxymethylaminomethane for Acidosis.—Nahas and Ligou (*Presse méd.* 67:1735, 1959) gave an intravenous infusion of trihydroxymethylaminomethane (THAM) to dogs with hypercapnic acidosis. The drug maintained a normal plasma pH level in the dogs but did not prevent the accumulation of CO_2. When this buffering agent was given, blood and spinal fluid pressures remained constant and a satisfactory diuresis was noted. Hypercapnic acidosis is the result of an increased concentration of hydrogen ions rather than of CO_2. The system may tolerate, with minimal physiological disorders, a concentration of CO_2 more than twice the normal concentration when the biological neutrality of the plasma is insured. In clinical trials THAM was well tolerated, had a low toxicity, and gave encouraging results in combatting acute acidosis.

Pyrvinium Pamoate for Oxyuriasis.—J. Biguet and co-workers (*Presse méd.* 67:1739, 1959) used pyrvinium pamoate to treat 45 children who had oxyuriasis. A seven-day cure was achieved in 20 with a daily dose of 2 mg. per kilogram of body weight, a three-day cure in 7 with a daily dose of 5 mg. per kilogram of body weight, and a one-day cure in 18 with a dose of 5 mg. per kilogram of body weight taken in a single draught. All stools were negative for pinworms during a six-week follow-up period after the treatment.

Histamine-Globulin Complex for Asthma.—A. Perrin and co-workers (*Presse méd.* 67:2013, 1959) reported their results in treating 50 patients who had severe asthma with subcutaneous injections of a histamine-globulin complex. Excellent results were obtained in 22, notable improvement in 14, and no improvement in 14.

Tuberculous Meningitis in Alcoholic Patients.—P. Perreau and M. Joulin (*Presse méd.* 67:1816, 1959) studied 15 alcoholic patients in a series of 217 patients with tuberculous meningitis. In 7 of the 15 the diagnosis was not made until the patient was comatose. The clinical signs of meningitis were modified by the association of severe liver damage and psychic disorders. The prognosis was far more severe than in children or patients not addicted to alcohol. Nine of these patients died. In others cure of the tuberculous meningitis was associated with aggravation of pulmonary, osseous, or renal tuberculosis in spite of intensive treatment. None of these patients was able to resume his work. Delayed diagnosis, frequent association with tuberculous visceral lesions, and impaired liver function were the main causes of the severity of tuberculous meningitis in the alcoholic patients.

Home Treatment of Tuberculosis.—Peumery and Le Quellec (*Presse méd.* 67:2015, 1959) studied 53 patients with early pulmonary tuberculosis who were treated at home. The medical supervision of these patients was analogous to that in a sanatorium. The disease was checked in 39, became less severe in 9, remained unchanged in 1, and was aggravated in 4. Aggravation was the result of alcoholism or insufficient treatment. When good sociological and psychological conditions exist, it is possible to treat early tuberculosis effectively at home even though surgical therapy may be required later.

ANP 235 for Disturbances of Consciousness.—R. Coirault and co-workers (*Presse méd.*, Feb. 6, 1960) gave *dimethyl-amino-ethylic* ester of parachlorophenoxy acetic acid (ANP 235) to 52 patients with mental clouding, stupor, and coma secondary to major neurosurgery or trauma. The oral dosage varied from 0.4 to 1.2 Gm. a day, but as much as 4 Gm. was given in a day without untoward effect. Intravenous injections were given slowly (1 cc. in 30 seconds). The drug acted as a neuronic stimulant. In some patients it was given in perfusions with hypertonic dextrose-levulose solution. The authors divided their patients into three groups: those with (1) recent disorders of consciousness, (2) disorders of long duration, and (3) syndromes involving endocrine complexes. Dramatic results were obtained in a 55-year-old patient who during the induction of anesthesia for an exploration of the posterior cranial fossa was in a critical condition with cardiovascular collapse which could not be controlled. He was given 500 mg. of ANP 235 in two intravenous injections in five minutes. One-half hour later he was out of danger and had a blood pressure of 120/80 mm. Hg and a pulse rate of 80 per minute. In the evening he was conscious and able to talk.

In the first group there were 23 patients with postoperative complications of major neurosurgical operations. One of these patients had been in a coma for nine days after the ablation of the right

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The items in these letters are contributed by regular correspondents in the various foreign countries.

frontal lobe and had a temperature of 40 C (104 F). Twenty-four hours after the administration of 4 Gm. of ANP 235 by gastric tube, the patient was conscious. The treatment was continued with decreasing doses, the patient regained consciousness, and his condition became good enough to permit an operation on the left frontal lobe. A 11-year-old boy who had been in a postoperative coma for three weeks received a daily dose of 800 mg. of ANP 235 by gastric tube; 48 hours later he regained consciousness, and on the fourth day he was able to feed himself. Another patient, in a coma for nine days after a hemispherectomy, regained consciousness gradually after receiving 400 mg. of ANP 235 orally. He became completely conscious on the fourth day.

The second group was composed of 25 patients who were in a state of deep obnubilation for 4 to 12 weeks after a major operation for cranial trauma. One of these patients had been in a state of cerebral anoxia for two months, with an attitude characteristic of decerebration and hypertonia of the extremities. His electroencephalographic tracing was flat. He was given an initial dose of 400 mg. of ANP 235, then 600 mg. daily. He regained consciousness and on the fifth day was able to follow a radio broadcast. His hypertonia improved. The total dose received by this patient, who was in excellent health when last seen, was 40 Gm. The authors believe that the concept that a flat electroencephalogram indicates a bad prognosis for regaining consciousness and obtaining long survival should be revised.

An unexpected result was obtained in a patient who remained in a deep stupor for two months after a cranial trauma. Under the administration of ANP 235, starting with a dose of 1,200 mg. daily and gradually decreasing the dosage to 400 mg. daily, the patient regained consciousness. His general condition was completely transformed within one month.

The third group comprised patients with syndromes associated with complex endocrine disturbances. In these patients, besides the effect on consciousness, ANP 235 acted favorably on the central mechanisms of endocrine and metabolic control at the level of the hypophysis and the hypothalamus. One patient in this group had a polyuropolydipsic syndrome after a three-week post-traumatic coma. After 11 days of treatment with a dose of 400 mg. of ANP 235 the diuresis was stabilized at 1,500 to 2,000 cc., the mental state was improved, and the patient was able to resume his occupation.

A more complex condition was observed in a 47-year-old man who after an operation for craniopharyngioma was in a deep coma for 30 days, with a spontaneous temperature of 32 C (89.6 F). The patient's condition was maintained with ACTH, cortisone, and thyroxin. Then the hormonal treatment was suspended and ANP 235 was given by gastric intubation. The patient came out of coma on the 5th day of treatment and became conscious on the 10th day. The authors stressed the fact that ANP 235 did not cause oliguria in patients who were free from diuretic disturbances. On the other hand, they did not observe hypercorticism. ANP 235 was also of great value in the preoperative and postoperative treatment of patients with paralysis agitans. Because of its beneficial effects on the cardiovascular plane, even aged patients can now have surgical treatment. ANP 235 is not toxic. The duration of the treatment reported varied from eight days to six months without any untoward reaction. This therapy is, however, contraindicated for patients with a progressive encephalitic infection.

GERMANY

Prevention of Kernicterus.—Dortmann and coworkers (*Arch. Kinderh.* 159:258, 1959) stated that until now the only promising treatment of icterus gavis neonatorum has been exchange transfusion. Failures (when the child's life could not be saved or kernicterus could not be prevented) have been associated with the child's age. The age limit was postulated as three to nine hours, but a definite limit could not be found, although the prospects of success appeared to be the better the earlier the child was treated. Knowledge of the pathogenesis of kernicterus and of the fact that the pathological manifestations of kernicterus clinically correspond to a bilirubin encephalopathy have suggested new therapeutic measures. Bilirubin encephalopathy occurs when pure (indirectly reacting) bilirubin exceeds a level of about 20 mg.%. According to recent research, an enzyme of the liver cells couples the pure bilirubin to glucuronic acid, whereby the water-soluble, excretable bilirubin diglucoronide is produced. This enzyme activity becomes fully effective only after birth, in mature neonates on about the fifth day and in premature infants on about the eighth day.

The aim of treatment must therefore be to tide the patient over this period, which shows why a single exchange transfusion may not suffice to avert the danger of bilirubin encephalopathy. The bilirubin level should be checked at brief intervals, every few hours if necessary, so that a second exchange transfusion may be given as soon as the level increases. One of every five patients required a second exchange transfusion, but some infants tolerated much higher bilirubin levels without ill effect. Since one does not know which infants, apart from the premature, are endangered, one should not wait but should repeat the exchange transfusion. The border level of 20 mg.% of bilirubin is not valid for the first transfusion. Levels this high are rare in the first hours of life; this value is only the guide for a further exchange transfusion. A further possibility for treating icterus gravis would be the conversion by drugs of the pure bilirubin into the water-soluble excretable form.

Heart and Circulation in Colds.—J. Schmidt-Voigt (*Therapiewoche* 9:186, 1959) stated that cardiac and circulatory disorders that can be definitely ascribed to a simple infection are not important but should not therefore be overlooked. Frequent sequelae of colds are arrhythmias, postinfective myocarditis, hypotension, and transient orthostatic disturbances. Postinfectious arrhythmias should be counteracted to prevent a neurotic or hypochondriac attitude. Best results were obtained with quinine, belladonna, phenobarbital, or quinidine. Postinfectious atrioventricular lead disturbances usually subside spontaneously. Apart from atropine or belladonna, a pill containing theobromine sodium salicylate, caffeine, sodium benzoate, phenylethylbarbital, strychnine nitrate, and atropine sulfate has proved valuable.

For a manifest myocarditis occurring in the course of a common infection, treatment until complete cure is indispensable. In addition to bed rest, strophanthine with a theophylline preparation for 10 days followed by digitalis until clinical cure proved valuable. Patients with severe cases may require antibiotics and adrenocortical hormones. For hypotension all measures that increase arteriolar tone should be used. Central nervous system stimulants and analeptics used for a limited period may give excellent results. Stimulating physical measures may be valuable adjuvants. When orthostatic disturbances occur, drugs with marked tonic effect on the venules should be given and the peripheral arterioles should be relaxed simultaneously.

Cortisone Thrombocyte Count.—K. Krug of Halle (*Medizinische* 36:1608-1610, 1959) stated that steroid therapy of thrombocytopenia has become common. It is generally supposed to inhibit antibody formation, which is followed by an increase in platelet cells. Rabbits were given a large dose of cortisone intramuscularly. Between the third and fifth day after injection the thrombocyte counts were, on the average, 59% higher (range 7 to 246%) than before the drug was given. Megacaryocyte counts indicated that a stimulating effect on these thrombocyte-forming cells probably takes place. Clinical studies also showed a beginning increase of thrombocytes a few days after treatment.

Adams-Stokes Disease.—M. Holzmann (*Therapiewoche* 9:222, 1959) stated that in severe attacks of Adams-Stokes disease transthoracic mechanical stimuli, such as blows over the precordial region in the rhythm of the normal heart beat, are always indicated. If they are ineffective, intracardiac injection of 0.5 to 1.0 cc. of a 1:1,000 solution of epinephrine, 20 mg. of caffeine sodium benzoate, or isopropyl levarterenol into the left ventricle is required. Cardiac massage, if the patient is not already on the operating table, is indicated only in exceptional cases. What treatment should be used in patients with frequent attacks of Adams-Stokes disease depends on whether the patient has total cardiac arrest, pancardiac paralysis due to sinus node arrest, total sinoauricular block, the ventricular form of paralysis with total atrioventricular block, or partial atrioventricular block.

In total cardiac arrest the aim of treatment must be reduction of the vagal tone or stimulation of its sympathetic opponent by atropine, Bellafoline ephedrine, Sympathol, or isopropyl levarterenol For obstinate cases local cocainization, local alcohol injections, and eventually extirpation of the reflex-conducting nerve fibers are indicated. The form of ventricular paralysis with total or partia atrioventricular block is now successfully treated with isopropyl levarterenol and the electric defibrillator. In clinical treatment injections or infusions of sodium lactate have also proved valuable

The tachysystolic form of Adams-Stokes disease is treated with such frequency-lowering drugs a quinidine, quinine, and procaine amide. Ventricula flutter can also be relieved by them, but ventricula fibrillation proves refractory to them and the electric current presents the last recourse. A difficul problem is presented by the mixed forms. Not a frequency-lowering drugs are suitable. Isopropy levarterenol and electrical control have been found best. Prophylaxis must be directed against all activities that are likely to elicit the attack. Attack associated with the premenstrual phase are counteracted by hormonal treatment. Continuous drug prophylaxis is hardly suitable for patients in whom attacks are infrequent, but it is indicated for thos in whom attacks occur several times a year. In such patients isopropyl levarterenol is most suitable.

Fluorescent Cytological Test.—L. von Bertalanffy (*Klin Wchnschr.* 37:469-471, 1959) stained vagina smears with acridine orange. On histological differentiation, the desoxyribonucleic acid had a green fluorescence and ribonucleic acid of the cytoplasm and of the nucleolus had a red fluorescence. Owing to their content of ribonucleic acid, cancer cells were easily recognized on only slight magnification. A comparative examination of 598 selected female patients, including 390 with atypical epithelium and 58 with carcinoma, with the acridine orange method and the use of the Papanicolaou technique showed that the two are equally accurate. In a group of 1,750 randomly selected patients who were checked by biopsy, the acridine orange test proved superior as far as false-positive results were concerned. Further advantages of the acridine orange test were that it was cheap, simple, clear-cut, and quick. It seemed to be preferable for mass examinations and gynecologic office consultations.

Prednisolone for Tuberculosis.—U. Baldamus and E. G. Ewert of Berlin (*Deutsche med. Wchnschr.* 84:1625, 1959) stated that steroid hormone in addition to standard treatment may be of great value in the treatment of patients with active pulmonary tuberculosis. As in other infectious diseases, the decisive factors are the potent anti-inflammatory effect and the prevention of undesirable reactive tissue changes. The main indications for steroid treatment in pulmonary tuberculosis are disseminated hemotagenous tuberculosis such as meningitis and miliary tuberculosis, acute pulmonary tuberculosis with severe hyperergic reaction, treatment-resistant progressive tuberculosis of the lungs, and extensive exudative pneumonic processes.

The authors gave prednisolone to 85 patients with extensive pulmonary tuberculosis, to 8 of them immediately after the disease had been diagnosed and to 57 with acute exacerbations of older processes. All had extensive bilateral tuberculosis with a poor prognosis. An initial dose of 20 mg. intramuscularly was repeated daily. After five days it was decreased by 2.5 mg. daily to a maintenance dose of 5 to 10 mg. usually given by mouth. The average duration of treatment was three months. In 25 patients the temperature returned to normal, and in 7 hemoptysis ceased. Radiographic results showed excellent regression of the tuberculosis in 35, good in 29, and poor in 21 patients. The sedimentation rate declined in 56 patients; the sputum became negative for acid-fast bacilli in 28 and remained negative in 7; in 50 it remained positive. The average increase of weight was 3.7 kg. (about 8 lb.). The prednisolone treatment had no essential effect in 28 of the patients. None of 14 patients who were given the drug to save their lives died. The ideal indication for hormone treatment was present in a second group of 18 patients with distinct clinical and radiographic evidence of progress of the disease after several months of chemotherapy; 16 of them were markedly improved while the prednisolone was being given.

In a third group of 38 patients in whom tuberculostatic treatment had not effected definite improvement, 23 were definitely improved. Local treatment with prednisolone gave less convincing results; in most of the 10 patients thus treated it was not possible to differentiate clearly the hormonal effect from that of standard treatment. Sixteen patients were resistant to isoniazid before steroid treatment was started. Prednisolone had no effect on the bacterial resistance. Undesirable effects of the hormone on the course of pulmonary operations were not observed, but the preparation was discontinued five days prior to operation. Adrenocortical stimulation by ACTH was not required. In 21 patients operability was achieved only by pretreatment with prednisolone, at least in a shorter time than with chemotherapy alone. All 21 survived, and this success was ascribed to the prednisolone. No conclusion could be drawn with regard to reactivation of quiescent foci, since in all patients the disease was active. Tolerance was excellent to both oral and parenteral treatment. Euphoria observed in a few patients proved favorable. Chemotherapy should not be discontinued soon after the end of steroid treatment, and ambulant adjuvant treatment with the steroid should not be attempted. The poor response to prednisolone in some patients was probably due to concomitant diseases or to bacterial resistance.

Smallpox Vaccination.—W. Ehrengut of Munich (*Öff. Gesundh.-Dienst* 20:458-461, 1959) reported that, because of the danger of postvaccinal encephalitis in those being vaccinated at a later age than usual, all children coming for revaccination were checked for the presence of vaccination scars. In a series of 9,511 children 751 had no visible first vaccination scar, and of these 171 had a valid certificate of vaccination. These 171 children were vaccinated with the following results: 71 had a first vaccination reaction, 80 an immunity reaction, and 10 each an accelerated vesicular or pustular reaction. It was found out from the parents that 580 children without first vaccination scar (i. e., 6% of those coming for revaccination) had never been vaccinated. Some of them were exempted from vaccination, and the others were vaccinated with the parents' consent.

The fact that 80 of 171 children without a first vaccination scar had an immunity reaction after revaccination was surprising. The children had apparently retained sufficient immunity from the first vaccination nine years earlier, although it had not left a scar. The accelerated vesicular and pustular reactions in 20 other children also indicated a revaccination. The absence of a first vaccination scar in children who had been vaccinated before might be explained as follows: (1) the inoculation incision was very small either for cosmetic reasons or for fear of neurological complication; (2) because of a delayed reaction only very small vesicles formed, since either the vaccine had but little virulence or the child possessed a high degree of resistance; or (3) scar formation varied greatly from one child to another and did not parallel the degree of immunity.

The German statistics on smallpox showed that scarless children coming for revaccination possessed a certain degree of protection, as was confirmed by the low mortality among them during the smallpox epidemic in World War I. In Munich, only 1% of the children coming for revaccination had fraudulent vaccination certificates. The author recommended vaccination of children coming for revaccination but having no first vaccination scar only after the parents have been asked about the success of the first vaccination.

NORWAY

Group Treatment of Asthmatics.—Lange-Nielsen and Retterstöl (*Nord. med.*, Dec. 17, 1959) reported on their experiences with group treatment of asthmatics. They avoided taking a leading part in the sessions. At first the attitude of the asthmatics was reserved and expectant and lacked spontaneity. Later on they became more communicative and admitted that these meetings helped them to escape from a sense of social isolation. With only one exception, admission to hospital due to relapse was avoided. All of the patients succeeded in reducing their consumption of drugs, and their attitude to life became more harmonious. In another article Dr. R. Christensen stated that asthmatics suffer more from neuroses than their fellow beings.

Scarlatina.—Scarlatina had become so rare and had run so mild a course in Bergen that it came as an unpleasant surprise in the latter half of 1959 when this disease assumed epidemic proportions. Two cases were reported in July, 11 in August, 76 in September, 559 in October, 925 in November, and 821 in December. Though the disease still ran a mild course, its complications from time to time occasioned questions as to suitable treatment. Prof. J. Böe (*Tidsskr. norske laegef.*, Feb. 15, 1960) deplored the tendency of a large section of the public to chew penicillin tablets constantly. At the outbreak of the epidemic, the cases were so rare and ran so mild a course that such tablets seemed unnecessary. Later there was a justifiable call for them in view of public health considerations even in mild cases, but there was no need for large doses as the offending hemolytic streptococci had not become penicillin-resistant. Once penicillin has been given, treatment should be continued for 7 to 10 days in the hope of averting complications and spread of the infection to others. The patient who is intolerant of penicillin should be treated with a tetracycline, the action of which is more reliable than that of the sulfonamides. Isolation at home is preferable to admission to hospital because of the danger of cross-infection.

Surgical Treatment of Peptic Ulcers.—A series of 170 patients (153 men and 27 women) who underwent resection for peptic ulcers were sent questionnaires by Dr. E. Dingsör (*Nord. med.*, Feb. 18, 1960). The 159 replies revealed that the mean preoperative duration of the ulcers was 10.8 years. Th operation was a modified Billroth 2 with a shor afferent loop to the lesser curvature after closure o the upper third of the stomach. Retrocolic anast mosis was effected in most patients. There wer some serious postoperative complications but n deaths. After a mean observation period of 4.2 year good results could be claimed in 94.4% of the pa tients. The two patients whose ulcers recurre underwent a second resection with excellent r sults. All of the 14 patients found to be anemic, fiv of whom had a hemoglobin level under 70%, r sponded well to iron given by mouth. There ha been a steady rise in the frequency of resections f peptic ulcers, but the 5 to 15% failure rate, irrespe tive of the choice of technique, exposes this pr cedure to the criticism that its rationale is st obscure.

SWEDEN

Refugees.—In the past 40 years Sweden has r ceived 201,768 refugees, according to statistics pul lished by the Swedish Labor Market Board. A refugees who have so desired have been allowed t stay in the country, and practically all who arrive since 1950 are now Swedish citizens. The numbe of refugees entering Sweden during World War I and the years immediately after totaled 185,00 Among these were 40,000 Finns who were eva uated to Sweden during the German retreat fro Finland and 33,700 persons from Nazi concentra tion camps who were brought to Sweden in 194 through the relief work organized by Count Folk Bernadotte. A total of 9,921 refugees have bee transported to Sweden since 1950, among who were 1,011 with active tuberculosis and 1,946 rela tives of theirs. Sweden was the first country t accept such refugees and, according to the Swedis Medical Board, their treatment has had satisfactor results. In December, 1958, only 69 of them wer still under the supervision of the Board. Most ha recovered and were active on the Swedish labo market.

Polyestradiol Phosphate.—A new preparation of th high-molecular substance, polyestradiol phosphate was used with good results to treat carcinoma o the prostate in men and the menopausal syndrome and amenorrhea in women. Dr. Gösta Jönsson used it to treat a series of 175 patients with carcinoma of the prostate. Only one injection a month is required, whereas previous treatment methods required the patient to take a tablet every day. Professor Axel Westman used it to treat 80 patients with severe menopausal symptoms. The advantage of the new preparation is its comparatively long period of effectiveness; one injection remains active in these patients for three or four months.

UNITED KINGDOM

Medical Advice for Industry.—A North of England Industrial Health Advisory Service, based on the Royal Victoria Infirmary, Newcastle-on-Tyne, was formed under the direction of a small committee representing the University of Durham, industrial management, and the Trades Union Congress. It is linked with a teaching and research unit and the outpatient department of the infirmary, which is part of the University of Durham. The object of the service is not to treat casualties but to give general advice to industry on health problems. Advice will be given concerning patients absent from work for more than a month, and in such cases the general practitioner will be integrated in the scheme. There will also be an environmental service, covering investigations on health within the factory, hygiene, laboratory investigations, and information on relevant literature. The cost to the firms using the service will be about 30 cents per year per employee, which is estimated to be about 5% of the cost of an industrial casualty service. To make such a service pay it would need to cover 50,000 to 100,000 workers.

The Nuffield Provincial Hospitals Trust has donated $32,200 and King's College Students' Rag Trust has donated $8,400 to finance the scheme initially. The staff members of the Nuffield department of industrial health are giving their services in an honorary capacity. This aid should put the new service on its feet. It is estimated that an industrial hygiene laboratory will cost $35,000 a year, but this expense will be offset somewhat by charging fees for laboratory services. It is hoped that ultimately the service will cover a large part of the north of England. A similar service which has been in existence for several years at Slough, near London, has been a great success.

Unorthodox Treatment Not Negligence.—A doctor called to see a 15-year-old boy in a residential school diagnosed a mild attack of infective hepatitis, although the boy said that he felt well. A fat-free diet and bed rest were prescribed, and as the patient's condition improved he was allowed to get up after a week. Improvement continued, and as the boy felt well he was allowed to go home for a few days. On his return to school a week later he had a relapse which necessitated hospitalization. In spite of expert treatment the boy's condition deteriorated, and three years later he died from cirrhosis of the liver. The boy's father sued the hospital and the doctor for negligence, alleging that the doctor had treated the case too lightly, had allowed the patient up too soon, and had run unjustifiable risks by departing from orthodox treatment.

Expert witnesses appeared for both sides. For the plaintiff it was argued that the current textbooks and articles on the subject stated that a patient with infectious hepatitis should be kept in bed until the symptoms had disappeared. The judge said that writers of textbooks were dealing with the subject in general, not with a particular patient, and that they described the treatment of the average case. Something must be left to the discretion and judgment of the doctor on the spot. He is not dealing with an abstract case, but with a patient, and he has to bear the whole clinical picture in mind. The judge held that a general practitioner was entitled to use his common sense, experience, and judgment in dealing with a patient and that he should not be bound to the literal interpretation of what he read in a textbook. Any disease could start mildly and become serious, but if a case had an unfortunate end a doctor was not negligent if he did not form the opinion that it would be serious. Statements in textbooks were no substitute for the judgment of the physician in charge. Considering all the evidence, the judge ruled that the doctor was not negligent and that he was not guilty of an error of judgment. It was unfortunate that the patient's condition turned out to be as severe as it was.

Cardiac Status at Birth.—Due to the recent advances in cardiac surgery, early recognition and accurate diagnosis of congenital heart disease have become increasingly important. Hallidie-Smith (*Brit. Med. J.* 1:756, 1960) evaluated the cardiac status of 230 infants just after birth, with particular reference to the incidence and character of cardiac murmurs. Fifty-five of the infants were reexamined when they were between the ages of 6 weeks and 6 months.

The mean sleeping heart rate showed a significant increase between the 2nd and the 11th day, from 113 to 130 beats per minute. Splitting of the first and second heart sounds was clearly audible from the time of birth, and phonocardiography showed that the average interval between the two was 0.024 second. The incidence of heart murmurs, which were all systolic, increased as each day passed. By the eighth day the incidence was 77.4%, and systolic murmurs were still heard in 48 of the 55 infants (87%) studied. Most murmurs were short, of low or medium pitch, and soft or very soft. Systolic murmurs were detected in most infants examined antenatally by phonocardiography. It is thought that most of these murmurs persist into childhood and are functional in nature. Transient cardiac murmurs were heard in infants who were anoxic at birth or who had a severe respiratory infection. As fetal systolic murmurs were frequently recorded during pregnancy it seems that these are rarely due to congenital heart disease.

CORRESPONDENCE

TREATMENT OF POSTOPERATIVE ILEUS

To the Editor:—Your abstract of Motta Maia's paper (*J. A. M. A.* 172:384 [Jan. 23] 1960) is most timely since it sheds light on an old but seldom used method, the treatment of postoperative ileus with drugs. Results obtained in the past with several peristalsis stimulating drugs, such as hypertonic saline solution, vasopressin, and neostigmine, were so poor that the procedure was claimed to be of dubious value. Now Motta Maia brings back the same old recipe with a new powerful ingredient, ambenonium chloride; 1 cc., containing only 62.5 mcg. of the drug, produces a better response than a full milligram of the old neostigmine preparation.

Prophylaxis or treatment of postoperative adynamic ileus or urinary retention are so easily obtained with ambenonium chloride that after trying it one wonders if intubation is ever needed in the treatment of such conditions.

Our work, which followed the same lines as that of Motta Maia, has established the value of the old method of using ambenonium beyond any reasonable doubt (*Arch. hosp. univ.* 10:262 [May-June] 1958, and *Surgery* 46:1043 [Dec.] 1959).

Celso Bilbao, M.D.
J #554 entre 25 y 27
Vedado
Habana, Cuba.

URINARY CONTROL IN CHILDREN

To the Editor:—In The Journal, March 19, page 1256, Dr. S. Richard Muellner, in his instructive paper entitled "The Development of Urinary Control in Children," pointed out that children who fail by the age of 3 years to enlarge their bladder capacity become enuretic. He has described a rational method for enlarging the bladder capacity and thus stopping the enuresis in such children. Enuresis has always been a mysterious disturbance which physicians have had difficulty treating and which they have tried to correct through symptomatic treatment instead of trying to understand the cause, which seems to be psychological in nature. My observations indicate that enuresis reflects a disturbance between the parents and child. The parents, instead of encouraging the process of growth and development, unknowingly interfere with it.

In the first year of life the interest of the child is centered around its mouth. In the second year of life this changes to the muscular system and the activities involving elimination. Toward the end of the second year, if one observes a child closely, one sees that the interest is directed towards the genital region. It is through the inhibition of this latter stage that enuresis becomes chronic and growth is inhibited, which results in the lack of development of the bladder which Dr. Muellner has observed.

It has been my observation that children who develop enuresis have had excessive stimulation by the significant parent (the boy by the mother, the girl by the father) and, at the same time, complete inhibition by the mother of any genital masturbatory activity, which one can observe in the child between the age of 2½ and 3 years. It is necessary to have both of these factors present in order to produce an enuretic child. To test this six mothers whose children were enuretic were treated. The only treatment given the children was a suggestion to the mothers that they should reassure their children that they would outgrow their enuresis. Treatment of the mothers was directed toward the investigation of their excessive stimulation of their children and their attitudes about masturbation. Within a period of three to six months all the children developed bladder control.

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OPERABILITY

To the Editor:—May I presume upon your precious time to point out a few salient facts? Your excellent section labeled Correspondence has, it seems to me, been overflowing with controversial but often inaccurate letters of late. I am sure it is your wish to interest the reader by drawing him more fully into debatable subjects, yet I fear you do yourself a disservice by printing such epistles as "Breast Cancer" (172:1083 [March 5] 1960). McWhirter, I believe, uses the word "operable" in Haagensen's original sense; i. e., according to his criteria for operability. This is the point. According to Haagensen's criteria many "inoperable" patients had five-year cures. Further, your reader mistakes the purpose of radiation therapy—that is, not to kill all cells but to retard growth and cause walling-off fibrosis, thus limiting their further growth or spread. He therefore asks "Does axillary radiation, then, not cure but merely postpone regional recurrence?", successfully bending the head of the nail at a 90° angle.

I remain, etc.

J. A. T.

I guess that I remain also—Ed.

New York City.

MEDICAL LITERATURE ABSTRACTS

INTERNAL MEDICINE

The Most Harmless, Most Practical, and Most Effective Method in the Prevention of Tuberculous Infection: Repeated BCG Vaccination of the Infant (Oral Impregnation) and Systematic Annual BCG Skin Test (Microrevaccination). M. Fourestier, J. Marsault, A. Blacque-Belair, and R. Robert. Semaine hôp. Paris 36:84-90 (Jan. 12) 1960 (In French) [Paris].

The authors report observations made between 1955 and 1958 in Montreuil, France, on 56 infants who were given BCG vaccine in the prevention of tuberculosis. The infants were given BCG vaccine orally in a single dose of 50 mg. before their first feeding in the morning on the 30th day of life. The vaccine was diluted in several cubic centimeters of boiled sugared water and given to the infant by spoon or bottle. No previous skin test for allergy was performed. This dose was repeated once a month for the following 5 months, the total dose being 300 mg. Thirty days after the last administration of the BCG vaccine, double skin tests for allergy, i. e., one ordinary tuberculin test on the right arm and a BCG test with 10 mg. of live tubercle bacilli applied to a scarification, 1 cm. long, on the left arm, were carried out. This double test is repeated systematically once every year. Eighteen of the 56 infants have been retested 3 times; 20, twice; and the remaining 18, once. The BCG test is considered an annual booster microrevaccination, while serving as a most sensitive test for the investigation of postvaccinal sensitivity to tuberculosis.

The double skin tests for allergy performed 30 days after the last administration of the BCG vaccine showed a negative tuberculin test and a positive BCG test in 20 of the 56 infants; both tests yielded positive results in 32 and negative results in 4. In 22 of the 32 infants with simultaneous positive results, the positive reaction of the tuberculin test was less intense than that of the BCG skin test; in 10 infants the reaction was equally intense, and the reaction of the tuberculin skin test was never more intense than that of the BCG skin test. In 6 of the 18 vaccinated infants who were reexamined for the 3rd time, the tuberculin skin tests were negative, and the BCG skin tests positive. In 11 infants both tests were positive, and in 1 both tests were negative. Up to date no case of tuberculosis occurred among the vaccinated infants. The authors believe that this method of vaccination is the least harmful, the most practical, and the most flexible of all the methods which have been suggested for the prevention of tuberculosis. The vaccination was well tolerated, and no side-effects were observed.

Acute Rheumatic Fever in Young Men: A Clinical and Epidemiological Study. J. D. H. Slater and S. Rosenbaum. Ann. Rheumat. Dis. 18:285-291 (Dec.) 1959 [London].

A clinical and epidemiologic study in young soldiers was undertaken to ascertain the incidence of initial and recurrent attacks of acute rheumatic fever; the pattern, frequency, and persistence of heart damage; and the importance of the preceding upper respiratory tract infection. Information was obtained from or about 379 soldiers who had had an attack of acute rheumatic fever while in the army. Ninety per cent of the patients were 17 to 21 years of age, and all except 3 were under 30 years old. Detailed reports were available on 2 groups, one (of 51 men) being treated by one of the authors and the other (of 67 men) being treated at the Cambridge Military Hospital. Information about the remaining 261 patients was obtained by examining official medical documents at the War Office. As a control group, a total of 1,179 soldiers, aged 17 to 22 years, were questioned personally to assess the frequency of a past attack of acute rheumatic fever as might be typical of such a general military population.

The average frequency of first attacks of definite rheumatic fever was found to be 0.59 per 1,000 young men living in a military community. A previous attack increased the risk of an attack about 42 times. Susceptible persons contracted rheumatic fever within the first few months of community living, which provides evidence that service conditions increase the risk of rheumatic fever. Why this should be is difficult to explain, for increased risk of the development of rheumatic fever cannot be adequately explained by greater contact with hemo-

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The place of publication of the periodical appears in brackets preceding each abstract.

Periodicals on file in the Library of the American Medical Association may be borrowed by members of the Association or its student organization and by persons in continental United States or Canada who subscribe to its scientific periodicals. Requests for periodicals should be addressed "Library, American Medical Association." Periodical files cover 1956 to date for English language and 1958 to date for foreign language journals. No photoduplication services are available. No charge is made to members, but the fee for others is 15 cents in stamps for each item. Only three periodicals may be borrowed at one time, and they must not be kept longer than five days. Periodicals published by the American Medical Association are not available for lending but can be supplied on purchase order. Reprints as a rule are the property of authors and can be obtained for permanent possession only from them.

lytic streptococci. New heart lesions were detected in 31% of the patients with rheumatic fever; persistent murmurs developed in 11%, being particularly common in patients who had had a previous attack.

Long History of Heavy Smoking as a Factor Causing Obstructive Pulmonary Emphysema. K. A. J. Jarvinen and K. Thomander. Ann. med. int. Fenniae 48:211-217 (no. 4) 1959 (In English) [Helsinki].

The incidence of long-continued smoking and certain other factors causing chronic bronchiolar irritation was studied in 2 carefully selected groups. The test group consisted of 42 persons with diffuse obstructive emphysema; the control group was comprised of 50 persons with healthy lungs. Besides the similarity in the method of selection, the 2 groups corresponded in age and sex distribution. Of the 42 persons in the test group, 36 were chronic heavy smokers (who had smoked a minimum of 15 Gm. of tobacco [15 cigarettes] per day regularly for not less than 10 years); of the 50 persons in the control group, only 19 were chronic heavy smokers. The correlation between obstructive pulmonary emphysema and chronic heavy smoking was even more striking among the women; 6 of the 11 women with obstructive pulmonary emphysema were chronic smokers, whereas only 2 of the 17 healthy women in the control group were smokers. Thirty-five of the 42 persons with obstructive pulmonary emphysema had chronic bronchitis, while none of the 50 persons in the control group had chronic bronchitis. Seven persons in the test group had a history of bronchial asthma for 10 to 46 years, and 2 had severe asbestosis.

Although the material studied was relatively limited, it does warrant the conclusion that long-continued and heavy smoking is one of the factors predisposing to the genesis of obstructive pulmonary emphysema. The correlation between chronic bronchitis and cigarette smoking has been found to be so close that even the frequency of bronchitis increased with the number of cigarettes smoked. Irritation of the bronchioles because of continual and heavy smoking leads to obstruction of the lumen and to the development of obstructive pulmonary emphysema.

The Magnesium-Deficiency Tetany Syndrome in Man. B. L. Vallee, W. E. C. Wacker, and D. D. Ulmer. New England J. Med. 262:155-161 (Jan. 28) 1960 [Boston].

Magnesium is second only to potassium in abundance as in intracellular cation, but while great strides have been made in the recognition of abnormalities in the metabolism of sodium and potassium, the same could not be said about magnesium. The development of a multichannel flame spectrometer, capable of measuring magnesium simply, accurately, and rapidly, has provided the means of overcoming this obstacle. The present paper describes a new specific clinical entity, human magnesium-deficiency tetany. This syndrome is virtually identical to that of hypocalcemic tetany, from which it can be distinguished only by chemical means. Its manifestations correspond almost exactly with those seen in magnesium-deficient animals.

The authors describe clinical and laboratory observations on 5 patients with tetany due to magnesium deficiency. Sustained losses of gastrointestinal secretions, prolonged parenteral fluid therapy, or severe infection acted as conditioning factors to produce the syndrome in previously malnourished persons. The clinical manifestations of the disease consist of tetany with carpopedal spasm or positive Chvostek and Trousseau signs, convulsions, athetoid movements of the extremities, and marked reaction to mechanical and auditory stimulation. In each case the concentration of magnesium in serum was markedly depressed, whereas the serum calcium concentration was normal. In all 5 patients with magnesium-deficiency tetany, parenteral administration of magnesium sulfate promptly and completely reversed the symptoms, signs, and chemical changes of the disease.

Diabetic Acidosis: An Evaluation of the Cause, Course and Therapy of 73 Cases. J. W. Runyan Jr. and D. Hurwitz. Ann. Int. Med. 52:55-86 (Jan.) 1960 [Lancaster, Pa.].

In the medical emergency presented by diabetic acidosis, a team effort and an organized approach has reduced the mortality. At a 2,000-bed municipal hospital, an approach to treatment based on current concepts was printed on a standard form, and was made available by the diabetes unit to all the medical and pediatric services. This report is based on observations on 52 patients who were admitted 73 times for episodes of diabetic acidosis. In 21 patients diabetes was recognized for the first time on admission. Among the remaining 31 patients, 16 had had previous episodes of acidosis, and 15 were acidotic for the first time. Not one of the patients had had control that could be classified as excellent or good. Most were casual in their approach to the disease. Five of the 31 patients with known diabetes had control classified as fair; none of these had had previous episodes of acidosis. The remaining 26 had poor control.

The most common precipitating factor of acidosis in those with known diabetes was the omission of insulin. This occurred in 20 patients; in one-half of these, emotional disturbances were related to the omission of insulin, and in the other half, negligence was at fault. The second most frequent precipitating factor was infection, present in 113 cases.

The infections were diverse in nature. Although infections were present on admission in many of the patients, the majority complained of symptoms directly referable to their uncontrolled diabetes. Twenty-six patients came to the hospital because of severe nausea and vomiting; 25 patients were brought in because of varying degrees of stupor or coma; 11 patients were completely unresponsive to external stimuli at the time of admission. Severe abdominal pain was the chief complaint in 9 patients.

Although fever was not uncommon in the patients with associated infections, a number, particularly those who were severely dehydrated and in shock, were found to be hypothermic. Tachycardia (pulse rate over 100 per minute) was usually present, and was more marked in the patients with severe acidosis. Overbreathing is a well-known accompaniment of diabetic acidosis. A review of the physical findings disclosed that the signs of dehydration were prominent. Dry skin was observed in 93%, flushing of the face in 74%, and soft eyeballs in 34% of the patients in whom note was taken of these findings. The odor of acetone was found on the breaths of 41% of the patients. True Kussmaul respiration was recorded in almost half of the patients, and again, like acetone odor, was twice as frequent among the patients with severe acidosis.

Immediately upon completion of urine and blood tests, patients were given 100 to 200 units of regular insulin subcutaneously. Intravenous administration of insulin was resorted to in patients in shock. Subsequent doses were 50 to 200 units of regular insulin subcutaneously at hourly intervals until improvement ensued. This program was modified according to the needs of the individual patients. Patients with moderate acidosis received an average of 560 units of ordinary insulin during the first 48 hours; patients with severe acidosis received almost double these amounts. For fluid replacement, hypotonic solutions were utilized. For initial hydration, 1 to 3 liters of the hypotonic solution, containing sodium (100 mEq. per liter), chloride (60 mEq. per liter), and lactate (40 mEq. per liter), were used. If there was sufficient improvement, 5% dextrose was added after from 4 to 6 hours. If improvement in blood and urinary sugar had not occurred after 3 liters of hypotonic solution, isotonic sodium chloride solution was administered, depending upon the electrolyte status. Less than half of the patients received potassium intravenously, and no severe hypopotassemia was observed. Potassium by mouth was added when it could be tolerated. The early use of long-acting insulin and early ambulation shortened hospitalization. Four deaths occurred in patients over 65 years. There were 9 instances of new or recurrent urinary tract infections associated with indwelling catheters, and the dangers of catheterization are highlighted. It became clear that the prophylactic use of antibiotics is useless, and that they should be used only for specific infections.

Observations on Erythrocyte Sodium and Potassium Concentrations in Patients with Kidney Disease. G. Manganelli and L. Pinto. Sett. med. 47:527-533 (Nov. 30) 1959 (In Italian) [Florence, Italy].

The authors measured serum sodium, chlorine, and potassium concentrations, as well as erythrocyte sodium and potassium concentrations, in 26 patients with kidney disease and compared them with those of 50 healthy persons. The nephrotic syndrome was present in 5 patients; chronic glomerulonephritis, in 14; and active or regressive acute nephritis, in 7. The changes of erythrocyte sodium and potassium concentrations took place more often and were more marked than the changes of serum sodium and potassium concentrations in this series of patients. It also appeared that the changes of erythrocyte sodium and potassium concentrations varied independently from the changes of serum sodium and potassium concentrations, and vice versa. It was not possible to establish a correlation between the changes of erythrocyte sodium and potassium concentrations and the type of kidney disease. There was no relationship between changes of the electrocardiographic patterns and the serum-erythrocyte electrolytic balance. There were no significant changes of chlorine with respect to sodium, except that hyperchloremia was observed in a few instances of the nephrotic syndrome. It appears from this study that the changes of erythrocyte potassium and sodium concentrations are a better index of the electrolytic balance in a patient with kidney disease than are the changes of serum potassium and sodium concentrations.

Positive Stool Guaiac Test After Meat Ingestion in Patients Who Have Undergone Gastrectomy. H. M. Spiro and H. L. Frucht. New England J. Med. 262: 188-189 (Jan. 28) 1960 [Boston].

In a patient who had undergone subtotal gastrectomy some years ago, the authors observed a persistently positive guaiac test while the patient was taking a regular diet; the test became negative when the patient stopped eating meat. Accordingly, they present studies demonstrating that after subtotal gastrectomy a rapid transit time or poor digestion may lead to the presence of meat in the feces and to a test for blood that is "falsely positive" in that it does not reflect intrinsic gastrointestinal disease. They conclude that, in the evaluation of a patient with subtotal gastrectomy for the presence of bleeding by the guaiac test, a meat-free diet is essential if occasional false-positive tests due to dietary intake are to be excluded.

SURGERY

Restenosis of the Mitral Valve: An Account of 50 Second Operations. J. R. Belcher. Lancet 1:181-184 (Jan. 23) 1960 [London].

The author reports on 50 patients with mitral stenosis, who had undergone commissurotomy and in whom reexploration of the mitral valve was carried out. There were 29 patients with "false" restenosis, the condition being defined as that which might follow inadequate commissurotomy; in these patients, although considerable improvement often followed enlargement of the orifice, the cups remained in apposition; as a result, the valve orifice was likely to decrease in size again, and so lead to the return of symptoms. In 17 patients "true" restenosis was observed, which might occur when at least one commissure had been fully opened at the 1st operation. In the remaining 4 patients the size of the orifice had changed little since the 1st operation. In 31 of the 50 patients the author had performed the original commissurotomy; these patients were derived from a series of 294 patients, subjected to valvotomy and followed up for a period ranging from 1 to 7 years, an incidence of 11%. Of the 50 patients, 46 were followed after the 2nd operation from 6 months to 3½ years. The operative mortality for the reexploration was 8%, which was a little higher than that of 5.5% for the primary valvotomies. Of the 42 surviving patients, 8 obtained excellent results; 17, good results; 10, fair results; 4, poor results; and there were 3 late deaths. Thus, more than 50% of the patients obtained a satisfactory increase in exercise tolerance, a result almost as good as that from the 1st operation, and in 11 this has been maintained for more than 2 years. In the diagnosis of restenosis, a detailed report of the 1st operation is important. The transventricular method of valvotomy has proved advantageous.

One Hundred Cases of Intracavitary Thrombosis in Patients Operated on for Mitral Commissurotomy. P. H. B. de Anda, M. J. Reinhold, and P. Fiamberti. Gac. méd. Mexico 89:905-918 (Nov.-Dec.) 1959 (In Spanish) [Mexico, D. F.].

Among 759 patients who underwent commissurotomy at the Instituto Nacional de Cardiologia de Mexico between 1952 and 1958, 100 (7.6%) had intracavitary thrombosis ascertained during the operation. These 100 patients were studied as to the presence of cardiomegaly, preoperative complications, and diagnosis and course of the disease. Four hundred ninety-six patients without intracavitary thrombosis at the time of the operation were studied as a contratest group. The following conclusions were drawn: The diagnosis of intracavitary thrombosis may be suggested, but not made with certainty, on the basis of atrial fibrillation and cardiac insufficiency of long duration. Atrial thrombosis, a mitral orifice smaller than 1 sq. cm., and absence of rheumatic activity were observed in the great majority of the patients. About 50% of them had a favorable long-term course, which in itself is an indication that a suspected intracavitary thrombosis should not prevent surgical treatment, in spite of the greater risk involved in the presence of this complication. Eighteen patients in this series died. Only 7 deaths were a consequence of surgical accidents. Most deaths occurred as a result of cerebral or aortic embolism, or of mitral tamponade.

A Follow-up Study 14 to 20 Years After Ventriculocisternostomy. A. Torkildsen. Acta psychiat. et neurol. scandinav. 35:113-121 (no. 1) 1960 (In English) [Copenhagen].

The author performed the first ventriculocisternostomy in Oslo in 1937. Since then, 3 groups of patients—the 1st with tumors in the pineal gland, the 2nd with tumors in the 3rd ventricle or infiltrating the walls of this ventricle outside the pineal gland, and the 3rd with occlusion of the aqueduct of Sylvius—were subjected to ventriculocisternostomy. Fourteen of these patients were alive by July 1, 1945; 3 were patients in the 1st group, 5 in the 2nd group, and 6 in the 3rd group. One patient in the 1st group, surviving in 1945, is still alive 20 years after the operation; he is in good health, working as a teacher. The 2nd patient in this group died 10 years after the surgical intervention, apparently because of the neoplasm, but was capable of working until the last year of life. The 3rd patient died 4 years after the ventriculocisternostomy because of metastases from a pinealoma.

Two of the 5 patients, surviving in 1945 in the 2nd group, are alive now, 20 and 17 years, respectively, after the operation; both are in excellent health. One patient lived 8 years after the operation and was capable of working until shortly before death; another patient apparently was in good health during the 7-year period prior to death; a 3rd patient who died after 5 years was seriously disabled during most of the postoperative period. Of the 6 patients in group 3 who were alive in 1945, 3 are alive now, 18, 17, and 14 years, respectively, after the ventriculocisternostomy. All are in good condition, are capable of working, and have not had symptoms of recurring intracranial hypertension, although one has some mental retardation. The remaining 3 patients have died since 1945. Cerebrospinal rhinorrhea occurred in one who died 4 years after the operation; a few days before death there were symptoms which may have been due to intracranial hypertension. Autopsy revealed occlusion of the drain which had been introduced at the time of operation, this being the only patient in the series known to have such postoperative occlusion. The cause of death, however, was diabetes mellitus. One patient died of bilateral pulmonary tuberculosis 10 years after the operation, and another died of unknown cause 4 years after the operation.

Thus, 6 of the 14 patients surviving in 1945 are still alive, and all of them are in good condition. Concerning the technique used in ventriculocisternostomy, the author now passes the tube extradurally, but intracranially, down to the cisterna magna. No other changes in the operative technique have been made.

Catheterization of the Left Side of the Heart: A Key to the Solution of Some Perplexing Problems in Cardiovascular Diagnosis and Management. E. R. Kelly, A. G. Morrow, and E. Braunwald. New England J. Med. 262:162-167 (Jan. 28) 1960 [Boston].

This report is concerned with the usefulness of catheterization of the left heart in the clinical management of 6 patients with unusual manifestations of relatively common forms of heart disease. In each, the definitive diagnosis and a rational therapeutic plan could be established only with the help of catheterization. The 1st patient presented with severe congestive heart failure, and no apical diastolic murmur was audible. There was electrocardiographic evidence of hypertrophy of the right ventricle, and it was assumed that the failure was primarily of myocardial origin. After catheterization, severe pulmonary hypertension, pulmonary vascular disease, or occult mitral stenosis appeared more likely. The presence of circulatory shunts was excluded by inert gas and indicator-dilution studies. However, the presence of pleural effusions and miliary pulmonary nodules suggested a systemic disease, and the relatively small size of the heart reinforced this belief. Catheterization of the left heart proved the presence of severe mechanical obstruction at the mitral valve, and the patient was benefited by mitral commissurotomy. There were 5 other patients in whom catheterization proved useful: one with hemodynamically mild mitral stenosis; one with "mixed" mitral lesions; one with myocardial disease simulating valvular disease; one in whom the severity of aortic stenosis was in question; and one with unusual hemodynamic sequelae of aortic valve disease.

The Ivalon Sponge Procedure for Myocardial Revascularization. A. Vineberg, T. Deliyannis, and G. Pablo. Surgery 47:268-289 (Feb.) 1960 [St. Louis].

The possibility that the myocardial network of vessels could rearrange themselves within the myocardial framework to form a sponge-like network of spaces and vessels, communicating not only with one another but also with extracardiac vessels, with coronary arteries and veins, and with the ventricular lumen itself, has been experimentally studied by the authors since 1956. The Ivalon-sponge operation was developed and tested on 54 dogs, 25 of which were contratest animals and 29 were treated. Myocardial ischemia was produced by placing constrictors around the origins of the anterior descending and circumflex branches of the left coronary artery. Removal of the epicardium and serous pericardium was done with a Beck scraper. Then sheets of Ivalon sponge, 1/16 in. (1.6 mm.) thick, were placed upon the front and back of the heart, where they were held in place by a few stitches of interrupted silk sutures. Twenty-two Ivalon-sponge-treated and 20 contratest animals were left for evaluation of the results, after excluding those that had had complications. Only 2 of the contratest dogs survived an 18-day period, the others apparently dying of myocardial ischemia. Nineteen of the 22 Ivalon-sponge-treated animals survived for 3 months or longer. Some of them were studied before and after being killed. It was obvious that the Ivalon-sponge sheets, applied directly to the bared myocardium, had in certain animals resulted in the development of a type of extracoronary blood supply sufficiently large to relieve the ischemia caused in the left ventricle by the constrictors.

The Ivalon-sponge operation was applied to a group of poor-risk patients with coronary artery insufficiency. Four of these patients had severe left ventricular failure and enlargement, and 4 were over 60 years of age. Eight patients underwent only the Ivalon-sponge operation, and 6 also had an artery implanation. There was no mortality in this series. The Ivalon-sponge-treated patients were out of bed on the 5th postoperative day, and at home within 2 or 3 weeks. The majority of the patients were free of pain at the time this article was written and seemed to be improving every day.

Diagnosis and Surgical Treatment of Constrictive Pericarditis. F. G. Uglov. Surgery 47:247-259 (Feb.) 1960 [St. Louis].

The numerous and varied symptoms of constrictive pericarditis result from limited diastole, which is responsible for the stasis in systemic circulation and the subsequent development of decompensation. Arrhythmia and tachycardia are common in the early stage, when they occur only on exertion. Physical examination frequently reveals cyanosis and edema of the face and swollen jugular veins. Ascites is often massive. The rise of venous blood pressure, enlargement of the liver, electrocardiographic findings of fall of curve voltage and low T waves, and indistinct outlines of the cardiac shadow in roentgenograms are among frequent signs and symptoms of constrictive pericarditis. The clinical picture is completed by increasing dyspnea, weakness and easy fatigability, and pain in the epigastric region. Kymographic findings are helpful in the diagnosis and selection of the proper operative approach to the heart. Operative intervention is imperative once the diagnosis has been made.

The author performed 50 operations for constrictive pericarditis with the following approaches: intracostal transpleural (1); parasternal with resection of costal cartilages and sternum (3); transbipleural (24); and flap incision (22). Sixteen of the 24 patients operated on by the transbipleural approach obtained good results, and 4 obtained marked improvement. These results were maintained for periods of 6 months to 6 years. Four patients died one month after the operation. Most of the 22 patients who underwent resection by the flap incision technique were poor surgical risks. Ten of them showed considerable improvement, 8 made good recovery, 3 had slight improvement, and 1 died. Evaluation of early and late operative results indicates that the flap incision is superior to other methods. This type of incision, which was developed by the author, begins at the level of the midclavicular line, extends along the lower margin of the 2nd rib to the right of the midsternal line, then goes along the right border on the midsternal line downward as far as the 6th intercostal space, and along the latter to the left up to the midaxillary line. A musculocutaneous flap is dissected, exposing the sternum, rib cartilages, and distal sections of the 2nd to 6th ribs.

The author's experience suggests that the results of operative intervention in constrictive pericarditis are in direct relation to the amount of the resected pericardium and the completeness of the decortication of large vessels from the pericardial ring constricting them. The transbipleural approach affords vast possibilities for the surgeon, since he can remove the whole pericardium, although in extensive denudation of the heart acute cardiac dilatation is a potential danger during the early postoperative period. This approach should be used mostly on patients with scarring deformation about the inferior vena cava necessitating resection, for the access to the inferior vena cava is difficult from the left flap incision. For all other sections of the heart the method of flap incision is advocated, because it is less traumatic and provides good results in both the early and the late postoperative periods.

The Influence of Clorpactin WCS-90 on the Bacterial Complications of Surgery.

M. K. DuVal and F. H. Howard. Surgery 47:210-216 (Feb.) 1960 [St. Louis].

A study of the effects of Clorpactin WCS-90, a nontoxic, nonallergic, water-soluble monoxychlorosene, in preparing the skin and irrigating the wound at the time of operation, was made over a period of one year and included 1,000 patients. The series comprised 533 males and 467 females of all ages, from newborn infants to octogenarians. The experimental group was composed of 489 patients, in whom the skin at the site of operation was scrubbed for 5 minutes with a 4% Clorpactin WCS-90 solution in distilled water; as the operation proceeded, the wound was irrigated for a full minute with 300 cc. of the Clorpactin solution once every hour and again at the time of wound closure. In some cases irrigation of the peritoneal or the pleural cavity was done. Nondrained operative wounds were covered with sterile dressings for 48 to 72 hours, and then left exposed. The control group was composed of 511 patients, who underwent the same procedure, with use of a surgical soap containing hexachlorophene for scrubbing the skin and a sterile sodium hydrochloride solution for irrigating the wound.

There were 262 "clean" and 249 "contaminated" patients in the hexachlorophene-treated group, 275 "clean" and 214 "contaminated" patients in the Clorpactin-treated group. The incidence of wound infection was 4.6% in the clean and 9.8% in the contaminated patients of the control group, while in the experimental group these percentages were, respectively, 1.8 and 7.5%. Although the difference is not statistically significant, there is evidence of a protective effect of Clorpactin. Further observations showed that, when the contact time with Clorpactin during the irrigation of the wound is increased from 1 to 3 minutes, the rate of protection also increases. One significant difference was that in the Clorpactin series 75% of the infections occurred either in cases of peripheral vascular surgery, in which the blood supply was insufficient, or in cholecystectomies. This limitation of infection was not noted in the control group. The failure of preventing infection in peripheral vascular operations justifies the inference that no agent can be a substitute for good surgical technique and gentleness in handling tissue, especially in situations of compromised blood supply.

Results Obtained by Superficial Femoral Vein Ligation.

H. W. Keisker and R. F. Bowers. Surgery 47:224-229 (Feb.) 1960 [St. Louis].

A group of 158 patients underwent 308 superficial femoral vein ligations as an emergency procedure in different circumstances, such as clinical evidence of phlebothrombosis, indication that pulmonary embolus had arisen from leg thrombosis, and need for a prophylactic measure when there was a history of venous disease or when there were signs of imminent thrombosis. Ligations in patients receiving anticoagulant therapy were reserved for emergencies, such as failure of the therapy, recurrence of pulmonary embolus of thrombosis disease, presence of large granulating areas, or imminence of reoperation. There were 2 postoperative deaths (1.3%). Follow-up studies of 2 to 10 years were conducted on 124 patients from the original group of 158.

Thirty-eight patients had died of unrelated causes, and 34 could not be contacted. Fifty-seven of the remaining 86 patients were interviewed personally, and 29 were checked by a questionnaire letter.

Three patients demonstrated nonfatal pulmonary emboli, occurring, respectively, at 3 months, 7 months, and 9 years postoperatively. Vena cava ligation prevented any further pulmonary incidents in these 3 patients. Postligation pulmonary infarcts, occurring, respectively, at 3 months, 4 months, 5½ years, and 8 years after the operation, were suggested by observation of 4 other patients. Thirty-eight patients complained of severe swelling of the legs, and 10 complained of mild swelling. The great majority stated that they had no difficulty in walking as much as 1 or 2 miles. Ulcers of the legs were found in 10 patients, 3 of whom already had ulcers prior to the ligation. Induration was present only where there was severe swelling, or when it was associated with ulcers. Only 2 of the patients who were able to work normally before the operation became unable to resume a gainful occupation. Femoral ligation appears to be safe, has a low mortality and morbidity rate, and in this series was not followed by fatal pulmonary embolism.

NEUROLOGY & PSYCHIATRY

The Married Mental Defective: A Follow-up Study. C. H. Shaw and C. H. Wright. Lancet 1:273-274 (Jan. 30) 1960 [London].

The authors selected a random sample of 242 persons (120 men and 122 women, including 10 couples whose partners were both known mental defectives) in a study of the married mental defective in Sheffield, England. These persons were followed up systematically to see what success they had made of marriage, 197 (81%) of them eventually being traced. Of 122 defectives in whom the intelligence quotient (IQ) was recorded, 93 (76%) had an IQ of between 50 and 69; the IQ of 13 (11%) was above this range, and that of 16 (13%) was below. The mean age of marriage among the men was 22.2 years, compared with 25.2 years among the women. Twenty-six infants born of these marriages died, an infant mortality rate of about 73 per 1,000 live births. Thirty-eight divorces or permanent separations were met in the survey, equivalent to 20% of the total families traced; 9 marriages were obviously unsatisfactory even to the outsider. Nevertheless, most of the marriages seemed to be reasonably happy and stable, even when the families presented problems to others. Twenty-six families could be described as problem families in the sense that they had presented problems to several social agencies. The home environment seriously jeopardized the physical and mental development of the children. In 15 families one or more children had to be removed from the care of the parents, though the family was not necessarily split up at the time of the survey. Of the 10 families in which both husband and wife had been ascertained mental defectives, 5 were regarded as problem families; of the other 5 families, only 2 could be considered satisfactory, 1 of these being a childless couple.

The impression from the survey was that mental defectives tend to choose, or be chosen by, a partner of approximately their own intelligence level. Though families existed in which all the members were obviously mentally subnormal, usually they (the members) tended to show ranges of ability not so very different from the average. A little extra effort, if the ability were there, could make all the difference in enabling a family to manage its affairs in a way acceptable to the community. The size of these subnormal families was larger than the average, though the additional births were to some extent balanced by the number of infant deaths. The employment record of the defectives was fairly good, despite a hard core who contributed little or nothing to the support of themselves and their families. The proportion of men who had fallen foul of the police was rather high. Most had been dealt with under the normal penal procedure, though 13 apparently were admitted to an institution as a direct result of the offence. A fairly high proportion of the children found neglected were the offspring of defective parents who themselves had an unsatisfactory upbringing. Patience and forbearance will be necessary if the mentally handicapped are to live in the community in peaceful coexistence.

Follow-Up Study of 849 Men Admitted for Mental Disorders to the Psychiatric Ward of a General Hospital. H. Forssman and B. Jansson. Acta psychiat. et neurol. scandinav. 35:57-72 (no. 1) 1960 (In English) [Copenhagen].

The authors report on 849 men, 459 of whom had been admitted for mental disorders to the psychiatric ward of the main general hospital in Göteborg, Sweden, in 1947; the remaining 390 were admitted in 1952. In 1957 a 10-year follow-up study was made on 385 patients (84%) of the 1947 series, and likewise a 5-year study on 358 patients (91%) of the 1952 series. Of the 385 patients, 283 (62% of the original 1947 series) were given a personal psychiatric examination, and of the 358 patients, 298 (76% of the original 1952 series) were given such an examination. An attempt was made to study the mental conditions of the patients at the time of the reexamination and to trace back the course of any disability during the years since discharge from the psychiatric ward. The results were evaluated on social grounds, mainly on work capacity. An extensive objective social study was made of all the men covered by the follow-up.

It was found that, of the 385 patients from the 1947 series, 329 were alive and, of the 358 from the 1952 series, 335 were alive. Of the 329 patients, 216 (66%) were mentally healthy, or at least capable of working, and so were 245 (73%) of the 335 patients. These results correspond with similar results reported in the literature. Of the 329 patients, 132 (40%) and, of the 335 patients, 159 (48%) had a favorable outcome insofar as they had not been readmitted to any psychiatric ward or had had no mental symptoms that prevented them from working during all, or practically all, the time since their discharge. As would be expected, the patients admitted for the first time in 1947 or 1952 showed a better outcome than those who had been admitted before. This was clearly demonstrated by a study of the course of any disability. The final results in the alcoholic addicts, who represented 35% of the 1947 series and 23% of the 1952 series, did not differ much from those in the total series or from those in the total series minus the alcoholic addicts. Patients with alcoholism, however, appeared to be more prone to recurrences than the other patients.

The final results in patients with a reactive depression were distinctly better than those in the total series, while those in patients with endogenic depression did not differ from the final results in the total series. The patients hospitalized when they were of middle age or older had final results which were slightly worse than those obtained by patients admitted to the psychiatric ward when they were young.

Effect of Menstruation on Schoolgirl's Weekly Work. K. Dalton. Brit. M. J. 1:326-328 (Jan. 30) 1960 [London].

The author collected data on the effect of menstruation from a boarding school for girls in southeast England during the autumn term. A total of 1,560 weekly marks of the schoolwork were available for analysis from 217 menstruating girls, between the ages of 11 and 17 years. The adverse effect of menstruation on the normal schoolwork of these girls was evidenced by the finding that one in every 4 girls had a fall in weekly mark during the premenstrual period, followed by a rise after menstruation. It is appreciated that in times of stress the premenstrual symptoms are increased. It would appear, therefore, that on occasions of important examinations the handicap imposed by menstruation will be proportionately increased. About one girl in 6 in any examination entry will be in her premenstrual period and thus at her lowest intellectual ebb.

GYNECOLOGY & OBSTETRICS

Relationship of Hysterectomy to Chronic Arthritis. H. Kerr-Taylor. Rheumatism 16:17-19 (Jan.) 1960 [London].

In the course of a statistical investigation for different purposes, it was found that in a series of 100 women with a rheumatoid type of arthritis 1% had had to be subjected to hysterectomy. A figure of 3% was derived from 2 series of 100 women each of similar age groups, who had consulted general practitioners and had undergone various types of operations. On the other hand, of a similar group of 100 women who had osteoarthrosis, 21 had undergone hysterectomy. All groups consisted of a consecutive series of women who attended a clinic for rheumatic complaints, and who were unselected, apart from being over 45 years of age. The author was unable to find in the literature any mention that the absence of the uterus or pelvic surgical disorders has any activating influence on the development of osteoarthrosis, as these figures might suggest. The relationship of rheumatoid arthritis to hysterectomy is of no apparent significance, as the figure is not significantly different from the ones derived from 2 samples of normal population, although an abnormality in progesterone metabolism in rheumatoid arthritis has been reported.

In consideration of the possibility of a general constitutional derangement as a result of the hysterectomy, the series of cases were reanalyzed on the basis that the presence of clinically palpable Heberden's nodes on the terminal joints of the fingers might be some evidence of a generalized degenerative osteoarthritic condition. From the findings obtained, it would appear that some constitutional or metabolic change is induced by hysterectomy, which may have a positive relation to the pathogenesis of osteoarthrosis. Literature reports related to this problem are discussed, and the author points out, among others, that the constitutional changes brought about by hysterectomy may lead to the activation or induction of arthritic changes in persons genetically susceptible by reason of an inherited autosomal gene dominant in females. The endocrine shock, or, in fact, the removal of the uterus, has also to be considered in the light of the experimental arthritis produced by the anterior pituitary growth hormone, and the overactivity of the pituitary inferred from the overproduction of the gonadotropins after the age of 50. The possible disturbances induced by hysterectomy in the related endocrine systems should also be considered. The interrelationship of the hypophysis, the thyroid, and the suprarenal glands to menstruation is well known, and thus a disturbance may be induced by the sudden removal of the uterus. The author remarks that there is little evidence in generalized osteoarthrosis of other clinical features of a hypoestrinic state, especially as arthrosis is characterized by dense hypertrophic bone tissue in distinction to the generalized osteoporosis associated with a deficiency in estrogens and androgens. Further investigations of these endocrine relationships in the pathogenesis of osteoarthrosis seem warranted.

Pudendal Block Anaesthesia in Obstetrics: A Review of 510 Operative Deliveries. J. A. Goldman. Brit. J. Anaesth. 31:538-542 (Dec.) 1959 [Altrincham, England].

Goldman presents observations on 510 patients who were delivered operatively of 525 babies in the obstetric department of the Beilinson Hospital, Petach-Tiqvah, Israel, between 1955 and 1959. The complications of pregnancy or labor in which pudendal block was used included heart disease, pulmonary disease, diabetes, toxemia of pregnancy, severe myopia, blood dyscrasia, recent thyroidectomy or nephrectomy, previous cesarean operation, premature delivery, prolonged labor, fetal distress, deep transverse arrest, and persistent occiput posterior position. The methods of delivery used under pudendal block were: low forceps in 460 cases; mid forceps in 14; assisted breech delivery in 39; and breech extraction in 12.

The parturients were carried through labor under anesthesia induced by an intravenously administered analgesic "cocktail" of meperidine, promethazine, and levallorphan, or by intramuscularly administered meperidine alone. With this form of analgesia, when delivery was about due, many of the parturients were relaxed and drowsy, sleeping during intervals and waking slightly during contractions. A mixture of 1% lignocaine with hyaluronidase, 1,500 I. U., and 0.5 ml. of 1:1,000 epinephrine solution was used to produce anesthesia in the form of a pudendal nerve block. About 50 ml. of this solution was injected with the aid of a 10-ml. Luer-Lok syringe with a 6-in. 18-gauge spinal needle. A wheal was made in the skin on each side, and the needle was introduced about midway between the anus and the ischial tuberosity. Two fingers in the vagina located the ischial spine, and the course of the needle was guided toward it. About 10 ml. of the anesthetic solution was deposited near the inferior aspect of the ischial spine and around it, in order to anesthetize the pudendal nerve as it enters Alcock's canal alongside the pudendal vessels. The needle was withdrawn, and 5 ml. was injected under the skin along the inner aspect of the labium majus, to include branches from the ilioinguinal nerve. Five milliliters of the mixture was injected near the tuberosity, where branches from the posterior femoral cutaneous nerve pass. Finally, the perineum in the region of the fourchette and the episiotomy site were infiltrated with another 5 ml. This procedure was repeated on the other side. The plunger of the syringe was withdrawn each time before injection, in order to avoid accidental injection of the solution into a blood vessel. The whole procedure took about 5 minutes.

The results achieved with this form of pudendal block anesthesia were graded as excellent in 485 women, satisfactory in 15, and poor in 10. During and after injection of the anesthetic mixture the pulse rate, blood pressure, and respiratory rate were not altered. No significant increase in postpartum bleeding was noted. Secondary uterine inertia and uterine atony were rare. There were no local infections, and only one minor hematoma of the perineum was found, which, however, did not impair healing of the episiotomy. No other side-effects or complications occurred, but in one patient a short psychotic reaction supervened, most probably due to an overdosage of lignocaine. No maternal deaths occurred. There were 7 fetal deaths.

PEDIATRICS

Primary Carcinoma of the Liver in Infancy and Childhood: Report of 11 Cases and Review of the Literature. R. G. Shorter, A. H. Baggenstoss, G. B. Logan, and G. A. Hallenbeck. Pediatrics 25:191-203 (Feb.) 1960 [Springfield, Ill.].

The authors report on 7 girls and 4 boys with primary carcinoma of the liver, whose ages at the onset of symptoms and signs varied from 5 months to 13 years, and who were admitted to the Mayo Clinic between 1905 and 1958. The main presenting features in all the patients was a mass in the upper portion of the abdomen, and in 5 it was associated with an increase in the size of the abdomen. Loss of appetite and weight was noted. Pain was a factor in 5 patients, vomiting occurred in 4, and 1 patient had had an episode of black, tarry feces during the week before admission. In 2 patients the spleen became palpable during the terminal phase of the disease. Anemia of the normochromic and normocytic types occurred as a complication in 9 patients and was an outstanding feature in 3. Two of the patients had jaundice at some time during the course of the disease. Chest roentgenograms showed the presence of pulmonary metastasis in 2, and elevation of the right side of the diaphragm in the other patients.

The duration of life after the onset of symptoms varied from 2 months to 2 years in 10 patients who died. In one patient excision of the tumor was attempted at another hospital, and the child died 4 days after the operation of necrosis of the liver. Resection of the right lobe of the liver was performed in one patient. This child made good progress initially, but one month after the operation he was found to have multiple metastatic lesions in the left lung. Roentgenotherapy was used after thoracotomy had shown that resection was impossible.

Resection was performed in another patient who died 2 months later. In 6 patients irradiation of the tumors with roentgen rays resulted in initially good response in 4. No treatment was advised in 2 patients. Only one patient had a history of previous disease of the liver; this child had had a hemangioma of the right lobe of the liver 6 years before admission. No common factors of possible etiological significance were found in these patients.

In 10 patients the diagnosis was established by surgical exploration and biopsy of a wedge-shaped section of tissue from the tumor. In one patient the diagnosis was established by needle aspiration of the right lobe of the liver. Microscopic examination of the specimens revealed that 7 of the 11 tumors were primary carcinomas and 4 were mixed tumors. The presence of a sarcomatous-like stroma is considered necessary for the diagnosis of a mixed tumor in the absence of osteoid tissue, cartilage, bone, or muscle. It is also contended that the presence of osteoid tissue in any amount precludes the diagnosis of primary carcinoma and necessitates a designation of mixed tumor. All the tumors were considered to be malignant, and extrahepatic metastasis was observed in 7 patients. The tumors caused the deaths of 10 patients within 2 years from the onset of symptoms. In the remaining patient, although the child is alive, multiple pulmonary metastatic lesions are present.

The Use of Acetazoleamide in the Therapy of Salicylate Poisoning. R. C. Feuerstein, L. Finberg, and E. Fleishman. Pediatrics 25:215-227 (Feb.) 1960 [Springfield, Ill.].

Forty-five children, between the ages of 1½ and 12 years, were treated for salicylate poisoning on the pediatric service of the Baltimore City Hospitals between 1950 and 1959. A group of 27, whose average age was 2.7 years, were treated with a regimen consisting of acetazolamide and fluids administered intravenously. As soon as the patient was admitted, an infusion of a solution containing one part 1/6 molar sodium lactate in 5 parts of 5% dextrose in water (1/36 molar sodium lactate) was started intravenously. When a diuresis had been produced, usually within 2 hours, the patient received 5 mg. of acetazolamide per kilogram of body weight intramuscularly. Two more similar doses were given at 4-hour intervals. The solution of 1/36 molar sodium lactate was given in quantities of 100 to 200 cc. per kilogram of body weight during the first 24 hours of hospitalization. Supplements of potassium in the form of potassium chloride (2 to 4 mEq. per kilogram) were added to the solution given intravenously. Fluids were given orally ad libitum when tolerated. The remaining group of 18 patients, whose average age was 3.5 years, were treated with parenterally administered fluids alone.

A comparison of the results from the 2 groups showed that the regimen of acetazolamide and parenterally administered fluids is an apparently safe and effective means of enhancing salicylate excretion. The importance of starting treatment early is stressed. The reason for using acetazolamide is that alkalinization of the urine greatly enhances urinary excretion of salicylate. Raising the pH of urine by means of alkalinizing solutions alone is cumbersome because of the time lag, and is possibly dangerous because of the large loads of sodium that must be given. The alkalinizing action of acetazolamide on the urine is prompt and can be coupled with the administration of larger amounts of sodium lactate or sodium bicarbonate than might otherwise be safe. Conflicting evidence from animal experiments suggests caution in the application of this type of therapy.

Early Medical Care of Delinquent Children. R. W. Deisher and J. F. O'Leary. Pediatrics 25:329-335 (Feb.) 1960 [Springfield, Ill.].

In an attempt to investigate the role of the pediatrician and other physicians in the lives of a selected group of delinquent children, and to study the types of problems observed during the preschool period and the kind of medical care received, the authors interviewed the parents of 102 juvenile delinquents at the King County Juvenile Court in Seattle. The ages of the children ranged from 9 to 17 years, with an average of 14 years. There were 22 girls and 80 boys; all were Caucasoid, except 5 who were Negroid and 1 Mongoloid. By means of a structured questionnaire-type interview, an effort was made to determine: (1) whether these delinquent children had developmental problems which could be diagnosed; (2) whether the parent or parents were actively aware of existing problems; (3) whether professional guidance was sought in the attempt to remedy the problems; and (4) what type of patient-physician relationship existed. The parents were questioned specifically about the type of medical care received by their children, the guidance obtained from physicians, and the active interest displayed by physicians toward developmental problems. Objective data depicting the early home life of the children were also obtained, including the incidence of working mothers, and of fathers who were absent from home for considerable lengths of time, during the child's formative preschool years.

There was no significant correlation between the type of emotional or developmental problem and subsequent juvenile delinquency, which would serve as an early diagnostic clue to the predelinquent child. In general, it was found that both parents and physicians showed little appreciation of emotional and developmental aspects of early childhood. Moreover, even when such problems were recognized, there was a significant tendency to take no definitive therapeutic action to remedy the problems. The parents were apparently satisfied only with medical care given for specific illness or injury. The most prominent deficiency in the parent-child-physician relationship appeared to be related to the lack of interest shown by some physicians in problems of child development, and the lack of time for discussion about the specific problems involved. Varying degrees of parental rejection of the children were believed to be present in many of these cases. The authors received the subjective impression that in many families the children had been deficient in love and/or attention during the early years of development.

A parallel control study, in which the parents of nondelinquent children within the same age range and from similar environmental backgrounds were used, was not possible because of limitations of time and the difficulty in obtaining an adequate contratest group; consequently, definite conclusions cannot be drawn. It must be emphasized, however, that, as the physician in most cases sees the child and his family throughout the preschool period, he could be of considerable assistance in the early detection of behavioral difficulties, and could provide the help that is indicated.

Relationship Between the Concentration of Neutralizing and Complement-Fixing Antibodies in the Mother and the Newborn Infant. E. Segagni, N. Ansaldi, N. Nigro, and others. Minerva pediat. 11:1385-1389 (Dec. 8) 1959 (In Italian) [Turin, Italy].

The values of complement-fixing and neutralizing antibodies of 3 types of poliomyelitis virus were studied in the serum of 35 pregnant women just before labor and in the serum of their respective babies within the first 12 hours of life. None of the mothers had ever been vaccinated against poliomyelitis, and none of them in infancy had suffered from a clinically manifested form of acute anterior poliomyelitis (Heine-Medin's disease). Considering first the 3 types of neutralizing antibodies, the following conclusions are drawn from this study. The neutralizing antibodies, considered independently from the immunological values of their titers, were found present in a large number of mothers and in some of the infants. For type 1 poliomyelitis virus the maternal titers presented variations from a minimum of 1:2 to a maximum of 1:128, the most frequent value being 1:16 and the average value 1:29.6; the neonatal values varied from a minimum of 0 to a maximum of 1:16, the most frequent value being 1:8 and the average value 1:7.6. All the mothers and 33 of the babies presented neutralizing antibodies for type 1 poliomyelitis virus. Neutralizing antibodies were present in 33 mothers and 22 babies for type 2 poliomyelitis virus, and in 26 mothers and 23 babies for type 3 poliomyelitis virus. There was no simultaneous absence of neutralizing antibodies for all 3 types of poliomyelitis virus in any of the mothers or their children. The neonatal titer for each type of poliomyelitis virus was always the same as, or lower than, the maternal titer. There were many instances in which a mother with measurable titer of neutralizing antibodies had a baby with nonmeasurable titer.

The complement-fixing antibodies were present in a few cases only, and the titers were very low. Complement-fixing antibodies were absent simultaneously for all 3 types of poliomyelitis virus in many instances. Most of the mothers and infants with measurable titers of antibodies presented a partial type-specific immunity. The neonatal titer for each of the 3 types of poliomyelitis virus was the same as, or lower than, the maternal titer, and in some cases the positive maternal values corresponded to the negative neonatal values. The authors believe that vaccination of pregnant women against poliomyelitis would provide immunity for the mother as well as for the newborn infant.

THERAPEUTICS

Hypocholesteremic Effect of Benzmalecene. I. H. Page and R. E. Schneckloth. Circulation 20:1075-1078 (Dec.) 1959 [New York].

One approach to the problem of prevention of atherosclerosis is the prevention of hyperlipemia and, more specifically, hypercholesteremia. The authors report studies on a new compound that has been synthesized for this purpose, Benzmalecene [N-(2,3-di-*p*-chlorophenyl-1-methylpropyl)-maleamic acid (*a*-form)]. They investigated the effects of Benzmalecene on the serum cholesterol levels in 6 women and 13 men. Of the 19 patients, 10 had severe essential hypertension, and 2 presented the syndrome of malignant hypertension; 7 other patients exhibited hypercholesteremia or hyperlipemia. All hypertensive patients were on free diets at home except for moderate salt restriction. Five of the 7 patients with abnormal serum lipid patterns had followed a carefully controlled diet, containing 50 to 80 Gm. of fat as vegetable oil, for periods ranging from 6 to 18 months; the remaining 2 patients had eaten freely chosen foods. The dose of Benzmalecene was 250 mg. given by mouth 2 to 4 times daily after meals; the average daily dose was 750 mg.

It was found that Benzmalecene effectively lowered blood cholesterol levels in most hypertensive patients but with some weight loss. Cholesterol was lowered in some hypercholesteremic patients but not in all, and this occurred without weight loss. In 2 hypercholesteremic patients a sharp rise in triglycerides occurred, while the cholesterol-phospholipid ratio fell and the free-total cholesterol ratio rose. Liver function, as measured by the Bromsulphalein test after 4 months' treatment, had deteriorated in 8 of the 12 patients studied. Nausea, epigastric discomfort, and diarrhea were on occasion sufficiently severe to require withdrawing the drug. The authors believe that drugs such as Benzmalecene should be studied in animals for long periods and in a few select patients before they are used to prevent atherosclerosis.

Pempidine Tartrate in Hypertension. H. S. Mathisen. Nord. med. 62:1805-1808 (Dec. 17) 1959 (In Norwegian) [Stockholm].

In the 10 months up to May, 1959, 32 hypertensive patients were treated with pempidine tartrate. In 25 of the cases, in 14 men and 11 women, the treatment was applied for more than 2 months—average time, 6 months. It was started with chlorothiazide, possibly in combination with a rauwolfia preparation. The usual chlorothiazide dose was 250 mg. daily. After the basic medication the pempidine tartrate treatment was instituted. The daily dosage, ranging from about 5 to 30 mg., was divided into 3 or 4 doses. In these clinical tests pempidine tartrate was found to be an effective ganglion-blocking agent, which reduced the blood pressure on oral administration. In most cases there was an improvement in the electrocardiograms, with satisfactory fall in blood pressure, especially in the diastolic pressure in the standing position, and distinct improvement in the general condition. The side-effects were the same as with other ganglion-blocking agents, even with the careful dosage applied. The combination of pempidine tartrate and chlorothiazide was, on the whole, particularly successful, only small doses of each substance being necessary. The addition of a rauwolfia preparation and hydralazine was desirable in some cases.

The Use of Dithiazanine as a Mass Treatment for Intestinal Helminthiasis. L. Guerrero, J. Holguin, and D. Botero. Am. J. Trop. Med. 9:37-38 (Jan.) 1960 [Baltimore].

The authors mention earlier reports on the use of dithiazanine in intestinal helminthiasis, then present their own studies carried out in Barrio Castilla, in the city of Medellín, Colombia, because it is a poor section with deficient sanitary conditions. Families were selected at random, and one stool examination was performed by the Stoll quantitative method, prior to treatment, in order to determine the degree of parasitic infection in each person. After the drug had been given to the infected person, another stool examination was made (by the same method) after the passage of 4 to 6 days to determine the effectiveness of the treatment. Intolerance to the drug was observed and noted. A group of patients primarily infected with Strongyloides stercoralis were selected at a hospital, and a special study was made in them. Helminths were found in the stools of 316 (87.2%) of the 362 persons examined for their presence. The 4 commonest species were Trichuris trichiuria, Ascaris lumbricoides, S. stercoralis, and Necator americanus. Although 98 of the 273 patients whose feces contained helminths harbored only one of these species, the remaining 175 patients harbored 2, 3, or 4 different species, the total number of infections being 508. The patients, who ranged in age from 18 months to 68 years, were treated with dithiazanine for 8 days. The daily dose for those weighing less than 15 kg. (33 lb.) was 200 mg.; for those between 16 and 30 kg. (35 and 66 lb.) in weight, 400 mg.; and for those over 30 kg. in weight, 600 mg. The daily dosage was divided into 2 or 3 partial doses. Post-treatment examinations revealed eradication of 372 of the 508 infections (73.2%). In the remaining 136 infections the helminthic burden was greatly lessened, the average egg count per gram of feces being reduced from 9,637 to 2,280, that is, by more than 75%. Signs of intolerance to the drug were observed in 119 (43.5%) of the treated patients, but in only 8 were abdominal pain and vomiting so severe that it was impossible to give the full course of treatment. In all the other patients the symptoms of intolerance either disappeared spontaneously or could be counteracted with sedatives and antacids. The authors conclude that dithiazanine is effective for mass treatment of intestinal helminthiasis.

Iproniazid (Marsilid) in Cancerology. F. Branco. Arq. pat. 31:451-466 (Nov.) 1959 (In French) [Lisbon].

The author used iproniazid (Marsilid) as a therapeutic aid in the treatment of patients with cancer because of the antidepressive, analgesic, and anabolic properties of this drug. The results obtained in 40 patients show that iproniazid improves the patient's general condition and vitality, relieves the pain, stimulates the appetite, and leads to weight gain in a short time. In many cases it was possible to eliminate the administration of analgesics for more or less extensive periods. Eight cases of malignancy treated with iproniazid are reported. Fiv patients had Hodgkin-Sternberg disease, 2 ha multiple myeloma, and one had malignant melanoma. The results were satisfactory in the 5 patients with Hodgkin-Sternberg disease and in th one with malignant melanoma. No relief was obtained for the patients with multiple myeloma Secondary reactions were observed in 2 patients; they consisted of mild euphoria in one, and of temporary overexcitement in the other.

Clinical and Pharmacological Studies with a New Diuretic: Benzydroflumethiazide. A. Cassano, C. Costa, C. Cordova, and L. Nuzzolo. Riforma med. 73:1418-1420 (Dec. 5) 1959 (In Italian) [Naples].

Single normal doses of benzydroflumethiazide were administered orally to 4 groups of patients with heart disease, totaling 48 in number and aged between 15 and 68 years. Valvular cardiac disease was present in 22 patients; coronary myocardiosclerosis, in 20; and cardiorespiratory insufficiency associated with sodium and water retention, in 6. Single doses of 2.5 mg. of the drug were given to the 1st group of 8 patients, of 5 mg. to the 2nd group of 22 patients, and of 10 mg. to the 3rd group of 8 patients. Single successively increasing doses of 2.5 mg., 5 mg., and 10 mg., administered every 6th or 7th day, were given to the 4th group of 6 patients. Increased urinary output, being considerable in most instances, was observed in 38 patients. Diuresis was accompanied by a loss of body weight, ranging from 500 to 2,200 Gm. (approximately 1 to 5 lb.). The optimum single diuretic dose was 5 mg. The diuretic effect took place within the 1st hour of drug administration, reached its peak between the 6th and the 12th hour, and lasted for at least 24 hours. The optimum drug-free period between 2 successive doses was 5 to 7 days.

Hydrochlorothiazide in single doses of 50 mg., in alternation with single doses of 5 mg. of benzydroflumethiazide, with a drug-free period of 6 or 7 days in between, was administered to 6 cardiac patients who had retention of sodium and water. It was observed that the diuretic effect was similar in the 2 drugs and that the optimum dose of benzydroflumethiazide was much smaller than that of hydrochlorothiazide. Diuresis of sodium chloride was also copious, but that of potassium and carbonates was moderate. Benzydroflumethiazide was well tolerated, and no significant side-effects were observed.

Treatment of Barbiturate Intoxication, with a Survey of 311 Cases. L. E. Böttiger and J. Östman. Acta med. scandinav. 165:437-444 (no. 6) 1959 (In English) [Stockholm].

No fatality from barbiturate intoxication occurred among 311 patients treated for this condition in the medical department of the Karolinska Sjukhuset in Stockholm during the 5 years from 1954 to 1958. The group included 146 mild and 165 moderately severe or severe cases. (Intoxication was classified as mild when patients were conscious on admission, and as moderately severe or severe when they were admitted unconscious.) All the patients were treated according to the method introduced by Nilsson in 1951 and often referred to as the "Scandinavian method." This treatment stresses the importance of a free airway and of the prevention and treatment of shock, but it does not include the use of central analeptics.

Bemegride was used as an adjuvant during a 21-month period, the admitting physician deciding which patients should be so treated. Eleven of the 20 patients who received the drug had the severe form of barbiturate intoxication. The adjuvant treatment consisted in injecting, intravenously every 5 minutes, 50 mg. of bemegride and 15 mg. of amiphenazole in a 5% dextrose solution. The highest total dose was 1,800 mg. of bemegride and 570 mg. of amiphenazole. Available data do not give a clear picture of the mode of action of bemegride, but it apparently acted as a central analeptic without specific antibarbiturate properties. The patients' reflexes frequently returned, only to disappear if the treatment became less intensive. The effect was the same as the one obtained with other analeptics, e. g., picrotoxin and amphetamine, but the patients did not seem to regain consciousness earlier when bemegride was used. The authors regard bemegride as a central analeptic with a certain value for respiratory stimulation, but not as a specific antibarbiturate agent.

Intensive Treatment of Intestinal Schistosomiasis with Antimony Preparations. P. Carvalhaes and V. Carone. Rev. Hosp. clín. 14:467-474 (Nov.-Dec.) 1959 (In Portuguese) [São Paulo, Brazil].

Twelve patients with intestinal schistosomiasis were treated with 2 antimony preparations, stibophen (Fuadin) and antimony lithium thiomalate (Anthiomaline), administered during 2 alternate periods of 10 days. During the 1st period each patient received an intramuscular injection of 2.5 cc. of stibophen on the 1st day, then a daily injection of 5 cc. until the 10th day. During the 2nd period each patient received a daily intramuscular injection of 2 cc. of Anthiomaline. Feces were examined before and after the treatment, and rectal biopsies were taken after completion of the therapy, their number varying from 2 to 7 for each patient. A treatment designed to protect the hepatic function (with methionine, choline, and vitamin B complex) was associated with the specific treatment, together with a diet rich in proteins, carbohydrates, and vitamins and low in fat. Bed rest was required during the entire 20 days of therapy. Electrocardiograms, blood tests, and liver function tests were obtained for each patient. The criterion of recovery was absence of live eggs of Schistosoma mansoni in the feces and at least 2 negative biopsies after completion of the treatment.

The patients were followed up for periods that varied from 2 to 5 years. Eleven patients were cured. The only patient whose rectal biopsy still showed live eggs after the antimony treatment had received only half the dosage given the others. Leukopenia was observed in 5 patients, leukocytosis in 2, and eosinophilia in 7. Slight electrocardiographic changes were observed in 7 patients. Gastric disorder, anorexia, and general malaise were the main side-effects. The authors believe that intestinal schistosomiasis should always be treated, although several investigators disagree. They consider the antimony therapy satisfactory but believe that the drugs should be administered during hospitalization because untoward reactions have occurred.

BOOK REVIEWS

Safe Handling of Radioactive Isotopes in Medical Practice. By Edith H. Quimby, Sc.D., Professor of Radiology (Physics), College of Physicians and Surgeons, Columbia University, New York. Cloth. $4.50. Pp. 129, with 16 illustrations. The Macmillan Company, 60 Fifth Ave., New York 11; Brett-Macmillan, Ltd., 132 Water St., S., Galt, Ontario, Canada, 1960.

With the growing application of radioactive materials in medical practice, this short book on the safe handling of radioactive isotopes is of great value. Although it is not intended as a complete manual on radiation safety but merely as a supplement to the work of the radiation protection officer, it contains much useful information. After a brief discussion of the nature of radioactivity and radiation, diagnostic and therapeutic uses of radioisotopes are described. This section is followed by a discussion of radiation hazards, maximum permissible doses, monitoring, safety in a "hot laboratory" and hospital, waste disposal, and decontamination. This book was written for technicians, nurses, doctors, or anyone else working with radioisotopes in a hospital or medical setting. It should help to put radiation hazards associated with the medical uses of radioisotopes into proper perspective for radiation workers.

Joseph Royal, Ph.D.

Recent Advances in Public Health. By J. L. Burn, M.D., D.Hy., D.P.H., Medical Officer of Health and Principal School Medical Officer, City of Salford. Second edition. Cloth. $10. Pp. 370, with 54 illustrations. Little, Brown & Company, 34 Beacon St., Boston 6; J. & A. Churchill, Ltd., 104 Gloucester Pl., Portman Sq., London, W. 1, England, 1959.

This title is not misleading provided the author had his tongue in his cheek. The book, written in textbook style, presents the story of the National Health Service. The ideal public health team is described vividly. Any active practitioner of medicine can well understand and often sympathize with the health team idea. Give the author credit. He does state the objections to certain phases of the British plan in this textbook of socialized medicine. For the doctor needing assistance in organizing the health facilities of his community this book offers many useful ideas. In general the author describes public health as a concept including the study of the total environment of man and any modifications necessary to meet the needs of man. There are many provocative statements and quotations from learned observers over the years.

Nearly 100 years' experience has confirmed the opinion expressed by Lord Derby in 1866 that "health instruction is more essential than health legislation, for the best laws are a waste of paper if they are not appreciated and understood." Good health certainly cannot be imposed by statute. The World Health Organization made the following observation: "Very often the start for any scheme has to be made slowly and indirectly—by finding out what they are prepared to accept and do for themselves. The belief that people of all levels of education, of all races and creeds, can do much to solve their own problems is a fundamental factor in World Health Organization work." It is one we should not forget in our own approach to public health. A quotation from John Donne cited in this book should suffice to interest all of us in the British experiment: "And therefore never send to know for whom the bell tolls; It tolls for thee."

Herman N. Bundesen, M.D.

Diseases of the Chest—Including the Heart. Edited by J. Arthur Myers, Ph.D., M.D., Professor of Internal Medicine and Public Health, Medical, Public Health and Graduate Schools of Medicine, University of Minnesota, Minneapolis. Cloth. $34.50. Pp. 1015, with illustrations. Charles C Thomas, Publisher, 301-327 E. Lawrence Ave., Springfield, Ill.; Blackwell Scientific Publications, Ltd., 24-25 Broad St., Oxford, England; Ryerson Press, 299 Queen St., W., Toronto 2B, Canada, 1959.

No period in history has seen the development of such an effective armamentarium to prevent suffering and untimely death as has the past two decades. Drugs have become available to control most bacterial and fungal infections of the respiratory tract. Advances in bacteriology and cytology have improved diagnosis and made prompt specific treatment possible. Surgeons now repair cardiac abnormalities, both congenital and acquired, and bring about a return of the person's working capacity and essentially normal life expectancy. Anatomists have learned that pulmonary lobes are divided into individual segments, each of which can be removed as conditions warrant. Advances in anesthesiology have made the anesthetist the surgeon's most important ally. The chest specialist who did all diagnostic and therapeutic work alone no longer exists. Specialities have developed within specialties, which make team work necessary. Not all specialists are necessary in every case, but each one must be available on call.

Thus no one physician can grasp all that is known or can write more than a fraction of a volume on the thorax. Most of the contributors to this volume have had long experience in the subjects on which they have written. Each contributor is cognizant of the fact that nothing is final and that much remains to be done. Consequently, no single reviewer could accurately judge the massive content except to catalog it as a valuable textbook for anyone interested in the broad subject of diseases of the chest and heart.

Part 1 is concerned with diseases of the chest and incorporates 24 chapters with references. Part 2 covers diseases of the cardiovascular system. The editor justly pays tribute to the publishers and their staff. This book should find a valued place for the progressive student and practicing physician as it is well prepared and illustrated.

H. J. Corper, M.D.

Lymphocytes and Mast Cells. By Margaret A. Kelsall, B.A., M.A., Ph.D., and Edward D. Crabb, B.A., M.A., Ph.D., Professor of Biology, University of Colorado, Boulder. Cloth. $8. Pp. 399, with 31 illustrations. Williams & Wilkins Company, 428 E. Preston St., Baltimore 2, 1959.

Much has been written about lymphocytes, but relatively little is known about them. The same applies to a greater extent to mast cells. This monograph is an attempt to gather between the covers of a small book what has been written about these cells. The authors are well qualified for the task. They have been contributing to the subject individually and jointly for many years. The lymphocytes, plasma cells, mast cells, and certain other cells (eosinophils, neutrophils, monocytes, and glia cells) supply nutritive materials and regulate protein metabolism. The feeding function of these cells, the trephocytes, is the subject of the book. The general principles are presented in the introduction. The second chapter deals with lymphocytes and plasma cells. The mast cell is discussed in the next five chapters; the specific topics are structure, staining methods, distribution, histamine, capillary permeability, heparin, and hyaluronic acid. The following chapters pertain to the thymus, spleen, marrow, intestinal lymphoid tissue, inflammation, and wound healing. There is a bibliography of 1,142 items and a well-organized index. The black and white illustrations are instructive.

The authors have succeeded in amassing a wealth of information on a highly complex subject. A particularly valuable feature is that much of the material deals with information on animals which is not easily available. It is to be regretted that the organization of the material is not as good as it could be. One has the impression that the data have been thrown together in review fashion without sufficient cohesion and synthesis. Other minor shortcomings are the use of terms which, though used in the original publications, are not in use any more: for example, splenomedullary leukemia; references to antiquated editions of books; occasional lapses of style (for example, "young rats often made appreciable growth" [page 282]; and "several cells in inflammations include lymphocytes, plasma cells, mast cells"). There are occasional typographic errors; for example, repetition of a whole phrase at bottom of page 281. All these are minor and easily corrected details. The book should prove useful to students of the subject as an up-to-date compilation of our knowledge of this highly specialized field.

Israel Davidsohn, M.D.

Bone as a Tissue. Editors: Kaare Rodahl, M. D., Director of Research, Lankenau Hospital, Philadelphia, Jesse T. Nicholson, M.D., Chief, Division of Orthopedics, Lankenau Hospital, and Ernest M. Brown, Jr., M.D. Proceedings of conference held at Lankenau Hospital, October 30-31, 1958. Cloth. $16. Pp. 358, with illustrations. Blakiston Division, McGraw-Hill Book Company, Inc., 330 W. 42nd St., New York 36; 96 Farringdon St., London, E. C. 4, England; 253 Spadina Rd., Toronto 4, Canada, 1960.

This compilation is divided into four parts. Part 1 thoroughly reviews the problem of osteoporosis. The authors and chairman of this section do not agree as to the cause of the condition, but the vast amount of investigative research that is presented permits an intelligent clinician to attain a better understanding of the etiology of osteoporosis as well as a sound clinical approach. Part 2 covers the current understanding of the chemistry and morphology of bone. Part 3, "Ultrastructure of Bone," is of special interest to clinicians and to investigators because of the excellent illustrations of electron-micrographs and of the use of autoradiography in the study of bone. Part 4 reviews and brings up to date the present status of parathyroid and vitamin D physiology. The chapter on citrate metabolism is of special interest as the importance of such metabolism has not received much recognition in the clinical journals.

This book contains a vast amount of documented scientific information, but there are not many conclusions. The discussions at the end of each section greatly enhance the value of the publication and present many leads for further investigation. The volume should be of value for instructors, students, and clinicians who are interested in the physiology and development of the osseous and collagen systems.

Clinton L. Compere, M.D.

QUESTIONS AND ANSWERS

CAUSE OF ASCITES

To the Editor:—*What is the cause of ascites in a patient who has acute necrosis of the liver? At autopsy there was no definite cirrhosis of the liver, malignancy, or heart disease. The serum albumin level was normal, but the kidneys showed cloudy swelling, and there were many bile casts in the tubules. Clinically, the patient had azotemia and oliguria, but neither peripheral edema nor pleural fluid was present.*

M.D., Quebec.

Answer.—Ascites in liver disease is caused by an interplay of many physiological and anatomic aberrations. The factors which, in various combinations, influence the pathogenesis of ascites are as follows: portal hypertension, decreased plasma osmotic pressure due to hypoproteinemia, increased lymphatic exudation from the liver, increase of antidiuretic hormone, and increase of (sodium-retaining) adrenocortical hormone. If the serum albumin level was determined by the Howe technique its measure includes the alpha globulin in the albumin fraction, in which case some hypoproteinemia may actually have been present in this patient.

The major defect may be hormonal. An increase of aldosterone has been demonstrated to occur in patients with liver disease with ascites, and there can also be an increase of antidiuretic hormone. Both would combine to produce oliguria and sodium retention.

Renal failure accompanying hepatic disease has been termed "hepatorenal" syndrome (a cholemic nephrosis develops in patients with severe, prolonged jaundice). The degree of azotemia does not correlate well with either the degree or the duration of hyperbilirubinemia. Thus, the bilirubin may not be the primary damaging agent to the kidney. It is likely that a preexisting renal defect, perhaps vascular in nature, is present in a patient with the so-called hepatorenal syndrome.

DETERGENTS AS ALLERGENIC SUBSTANCES

To the Editor:—*A patient appears to be allergic to detergents but not in the usual fashion. His difficulty seems to be related to inhalation of the allergenic substance, as in a person who is allergic to the feathers in pillows. Exposure to the detergent substance retained in bed linen causes the patient to have intestinal distress which keeps him awake. Practically all soap powders and flakes contain detergents, and bed linens, if not thoroughly rinsed after being washed, retain small amounts of the cleansing agent on the fibers. The patient is allergic to many other substances, including certain foods. Do detergents cause allergic reactions by an inhalant type of allergen? If so, have other physicians encountered similar problems?*

A. E. Taft, M.D., Haverford, Pa.

Answer.—There appear to be no authenticated instances of patients having true inhalant allergic reactions to detergents. The possibility exists, however, since many simple chemical compounds (aspirin for example) can act as allergens, probably through the haptene mechanism. The patient described sounds more like a person who has severe ringing in the ears because of an intolerance to small doses of quinine which is not an allergic reaction but a hypersensitivity to the drug. Detergents in powder form may also act as nonspecific irritants to nasal or bronchial mucous membranes.

CHOICE OF BLOOD OR PLASMA FOR INFUSION

To the Editor:—*Is it permissible or desirable to treat a patient who has lost a great amount of blood by giving plasma rather than whole blood? What are the indications for the use of plasma?*

M.D., Wisconsin.

Answer.—A patient usually can withstand the loss of 1,000 cc. of blood, because the body can temporarily adjust to the lowered blood volume and the decrease in systolic blood pressure. When amounts of blood greater than 1,000 cc. are lost, the blood pressure is no longer maintained, and the oxygen supply to the vital centers is no longer adequate. A sudden hemorrhage of about 2,500 cc. may be fatal. Blood volume can be restored rapidly by the administration of whole blood, serum, plasma, or a suitable plasma volume expander.

The choice of plasma rather than of whole blood may be disadvantageous, however, because the volume of circulating erythrocytes may be insufficient for adequate transportation of oxygen. It is unwise to allow the content of hemoglobin to decrease to less than 9 Gm. per 100 cc.

The answers here published have been prepared by competent authorities. They do not, however, represent the opinions of any medical or other organization unless specifically so stated in the reply. Anonymous communications cannot be answered. Every letter must contain the writer's name and address, but these will be omitted on request.

After administration of whole blood the erythrocytes remain in the blood stream longer than any other component of the transfusion and thus produce a sustained increase in blood volume. Whole blood also increases the oxygen-carrying power of the blood.

If a supply of compatible whole blood is not available, a patient suffering from acute loss of blood must receive plasma or other fluid to support him until whole blood becomes available. The ideal procedure is to administer about the amount of whole blood that has been lost by the patient.

The chief indication for giving plasma is acute loss of plasma without the loss of erythrocytes, which occurs in conditions such as burns, acute obstruction or strangulation of the small intestine, and crushing injuries in which there is considerable local loss of plasma. Whole blood also must be administered to victims of burns to replace the loss of erythrocytes by way of hemorrhage, toxicity, and normal destruction.

CORONARY THROMBOSIS AND SMOKING

To the Editor:—*When patients who used to smoke have recovered from coronary thrombosis, are attacks more likely to occur in (1) those who resume smoking compared to those who do not, (2) those who confine themselves to cigarettes, (3) those who use only cigars, or (4) those who smoke pipes only?* *M.D., South Carolina.*

Answer.—There are, apparently, no statistically supported studies which might serve as the basis for a reply to the above questions. Information on these topics belongs in the category of opinion rather than that of statistically substantiated conclusions based on adequately controlled clinical observations.

EXERCISE AFTER INTRAVERTEBRAL DISK HERNIA

To the Editor:—*A 48-year-old man has had three episodes of ruptured intervertebral disk. Each time he was treated conservatively, with good results. Because of his sedentary work he would like to engage in some form of routine setting-up exercises. What restrictions on physical activity are usually recommended to patients with this condition?*

Richard M. Dawes, M.D., Gramercy, La.

Answer.—The conservative management of a patient with a herniated intravertebral disk, once the acute stage has been treated and the patient is relatively symptom-free, is divided into three parts, which are as follows: 1. Prophylaxis. The patient should refrain from all heavy lifting and from any sudden twisting and bending movements. Since many routine setting-up exercises consist of twisting or bending movements, they should not be done. The patient should be taught, when lifting objects, first to bend the knees and hips while he stoops to reach the object and thereafter to keep his back straight during the entire lifting process. Another activity to be avoided is driving long distances. The patient should be shown how to adjust his automobile seat to prevent excessive straight leg raising. 2. Physiotherapy. In place of routine setting-up exercises, the patient should be given a detailed exercise routine designed to strengthen the glutei, hip muscles, and spinal and abdominal muscles without the ordinary torsional and flexibility motions that are present in the setting-up routine. This selective exercise regimen should be carried out daily to the point of intolerance. It should not be a hit-or-miss program. 3. The use of a support to the back is often helpful and will remind the patient what not to do.

INFLAMMATORY CARCINOMA OF THE BREAST

To the Editor:—*What treatment is recommended for localized inflammatory carcinoma of the breast? A patient has had an area of inflammation in her left breast for about three months. The area surrounds the nipple; it is about 6 cm. in diameter, warm, and red, and it causes the skin to have a "pigskin" appearance. A biopsy specimen of the mass showed "highly anaplastic, poorly differentiated carcinoma, type undetermined, compatible with inflammatory carcinoma."*

John McCain, M.D., Wilson, N. C.

Answer.—The consensus is that inflammatory carcinoma of the breast should not be treated surgically. A recent exception to this rule was taken by Fitts (*Surg. Gynec. & Obst.* 107:95 [July] 1958). Usually the local lesion is treated by irradiation, and occasionally favorable results are obtained from oophorectomy, adrenalectomy, or hypophysectomy. Administration of androgenic or corticosteroid agents might be tried if ablative therapy is refused.

URETHRITIS AND TRIGONITIS IN WOMEN

To the Editor:—*A 42-year-old woman has chronic urethritis and trigonitis which has resisted all treatment. Dilation, with instillations of a mild silver protein preparation and of nitrofurazone, and therapy with urethral suppositories gave the patient only temporary relief. Can you suggest any further therapy?*

Gordon D. Anderson, M.D., Harvey, N. D.

Answer.—This condition affects a large number of women. The most common cause of resistant urethritis and cystitis is obstruction, with or without infected urethral glands, which accounts for the frequency of recurrence after dilation and other usual treatments. Infected urethral glands and hypertrophic changes in the urethral mucosa, in both the anterior and the posterior portion at the vesical neck, contribute to the trigonitis and cystitis. Urethral meatotomy, with excision of infected urethral glands and hypertrophic mucosa as well as transurethral resection of the vesical neck, has given effective relief in most instances.

PHYSIOLOGICAL JAUNDICE IN NEWBORN INFANT

To the Editor:—*The answer to the question in* The Journal, *Dec. 5, 1959, page 2035, on Physiological Jaundice in the Newborn Infant appears to be conservative, but one may disagree with the relatively rigid recommendations made with regard to the indications for exchange transfusion "—regardless of the cause—if the bilirubin concentration exceeds 4 mg.% at birth, 10 mg.% in the first 24 hours of life, 14 mg.% in the second 24 hours of life, or 17 mg.% at any time in the second to fourth day of life."*

A large percentage of babies falling into the above categories will spontaneously have a decline in the bilirubin concentration, and an exchange transfusion need not be carried out, if the physician is patient and evaluates the entire story, makes a physical examination, and obtains consecutive bilirubin concentrations of plasma at appropriately spaced intervals.

There are no convincing data showing that the full-term baby who has a bilirubin concentration even as high as 23 mg.%—but who otherwise appears normal—suffers risk of brain damage which is greater than the risk of an exchange transfusion. Unfortunately, all convincing evidence of the occurrence of brain damage in full-term infants whose bilirubin values extend from 20 to 30 mg.% is grouped together. Complications of exchange transfusion include acute hemolysis, infection, cardiac arrest, and death.

The physician who attends newborn infants is advised to have full knowledge of all factors which may influence the decision about the need for an exchange transfusion. The rate of rise of the bilirubin concentration is frequently one of the chief factors to be considered. The monograph by Allen and Diamond (Erythroblastosis Fetalis, Including Exchange Transfusion Technic, Boston, Little Brown & Co., 1958) contains an extensive bibliography. It should be kept in mind that new data and other forms of treatment may soon settle some of the present controversies.

Hans G. Keitel, M.D.
Jefferson Medical College of Philadelphia
1025 Walnut St.
Philadelphia.

The above comment was referred to the consultant who answered the original question, and his reply follows.—Ed.

To the Editor:—*The physician states correctly that the rate of rise of the bilirubin level is one of the principal diagnostic factors. The criticism of a rigid recommendation may be due to the fact that it was not made entirely clear that jaundice occurring in the first 48 hours of life is in no sense a physiological jaundice. It is the symptom of a grave hemolytic process which is due to incompatible antibodies, infections, or deleterious substances that endanger the life of the baby. The immediate danger of hyperbilirubinemia must be treated first and the etiological factors later.*

Not all the factors causing nuclear icterus are known. One factor is a bilirubin concentration (indirect) of over 20 mg. per 100 ml., although instances of its occurrence have been reported below this level. Furthermore, not all infants (possibly under 10%) will develop nuclear icterus above this level of bilirubin. There is no prognostic means to determine which 10 of 100 infants are going to develop the condition. Hence, it is a matter of extreme importance to treat all infants whose bilirubin concentration rises above this level.

It is true that it is seldom necessary to resort to an exchange transfusion, if the rate of rise of indirect bilirubin is less than 0.23 mg. per hour on estimations made on the infant's blood drawn at 8-hour to 12-hour intervals. Nevertheless, physicians are not justified in delaying treatment, because it is much more difficult to treat a patient for a high serum bilirubin level than to keep it from occurring. It must be remembered that the infant's entire body has been saturated with this pigment, while the exchange transfusion removes only that bilirubin which is present in the blood circulation. An early exchange transfusion, therefore, removes the principal source of bilirubin before it can accumulate in the tissues by removing the source of the bilirubin and the damaged circulating red blood cells (already made incompatible by the attached antibody). The earlier an exchange transfusion can be given, the less chance that higher concentrations of bilirubin will accumulate in the body.

The criteria for replacement transfusions can be accurately determined by bilirubin levels measured at various hours of life. It will be found that the danger levels as stated are well within their "zone of obligatory exchange transfusion" (Allen and Diamond, op.cit.). Some babies later will show a decrease in bilirubin below the predicted level, but they are few in number. Wheeler and Ambuel (Pediat. Clin. North America, *May, 1957, p. 395) stated that, in their hospital, 80% of those babies who had a cord bilirubin level above 4 mg. per 100 ml. eventually needed an exchange transfusion.*

WASHINGTON NEWS

Forand Bill . .
Backs Trade Name Prescriptions . .
Drug Warning Label Guide . .

COMMITTEE DELIBERATES COURSE ON AGING ISSUE

Behind closed doors, the powerful House Ways and Means Committee began its crucial task of deciding what type of aged health care measure to approve, if any, this session.

The two major plans before the panel were the administration's 1.2-billion-dollar program of a voluntary, federal-state aid scheme, and the Forand-type compulsory approach through the social security system. In addition, there was some consideration given to expanding the existing federal-state public assistance programs for the aged to spur further help for indigent persons in the medical-hospital care field.

While the House awaited the decision of the Ways and Means Committee, whose bills are seldom rejected by the full House, there were developments in the Senate.

Sixteen Democratic senators, including presidential hopefuls Senators John Kennedy (Mass.), Stuart Symington (Mo.), and Wayne Morse (Ore.), introduced identical legislation proposing a broad medical aid program, most of it under social security.

The bill would provide hospitalization and health care for all of the nation's retired older citizens. Most of the estimated cost—1.6 billion dollars—would be financed through a 0.25% hike in the Social Security tax on the employee and the employer, and 0.375% for self-employed persons. Surgical services would not be included, though these would be financed under the Forand bill.

Retired aged persons not eligible for Social Security benefits would receive similar benefits. Cost of this program would be borne from regular government appropriations to a federal medical insurance trust fund.

Chief sponsor of the legislation was Sen. Pat McNamara (D., Mich.), chairman of a special Senate subcommittee on problems of the aging. The Senator has advocated a compulsory government medical program for many months.

Vice-president Richard M. Nixon expressed his vigorous support of the administration's plan, and charged that the Democratic Social Security bills would "open the door for socialized medicine."

In a formal statement, he emphasized that the over-all difference between the two proposals "goes to the fundamental nature of our free society."

The Forand bill and similar plans would set up a great state program which inevitably would head in the direction of herding the ill and elderly into institutions whether they desired this or not," he said. "Such a state program would threaten the high standards of American medicine."

Meanwhile, Rep. Thomas B. Curtis (R., Mo.), a member of the House Ways and Means Committee, contended that members of both parties were pushing for an unneeded federal program of health insurance for the aged. The lawmaker said he was convinced from detailed studies that there are no indigent persons who need medical attention who cannot get it on a charity basis. As for elderly persons, "there is good health insurance available at reasonable rates."

Senate GOP Campaign Chairman Barry Goldwater (R., Ariz.) denounced the administration's plan as "socialized medicine" and a "dime store new deal."

Goldwater told the Senate the ultimate cost of the new plan will be "staggering" and prevent future balanced budgets.

Goldwater said Arthur S. Flemming, Secretary of Health, Education, and Welfare, could better have solved the medical problem by proposing "full deductions for taxes for any amount spent for medical care of anyone," plus full tax deduction of the costs of health plans by either an individual or corporation.

URGES DELAY ON AGED HEALTH CARE ACTION

A key member of the House Ways and Means Committee urged that action on all proposed federal health benefit plans for the aged be postponed until next year. In the meantime, Rep. Burr Harrison said the committee should conduct an exhaustive study of the various proposals during the congressional recess.

Harrison declared, "It is obvious from recent events that the nation will adopt a new and revolutionary expansion of the welfare state through the inauguration of a program of medical benefits.

"The Congress now has before it the Forand bill for limited hospital and surgical aid to persons receiving social security benefits; a proposal for limited hospitalization only; the plan of the President, endorsed by Vice-president Nixon, for sweeping medical benefits for the needy aged, financed out of the general treasuries of state and federal government; the American Medical Association proposal; and half a dozen other variations of the foregoing proposals.

"The only features which these proposals have in common is that they are all tremendously expensive; they all propose revolutionary change, and they are all complicated, uncertainly based and little understood by the prospective beneficiaries.

"The only one of these plans on which there has been a hearing, and on which the public has been allowed to express an opinion, is the Forand bill, which the committee rejected by a vote of 17 to 8.

"Any such vast new permanent program, costing billions a year, if drafted and launched in haste, without opportunity for public expression and in an atmosphere supercharged with election year politics, would be certain to be a monstrosity.

"I propose that the Committee on Ways and Means conduct full public hearings during the recess of the Congress this fall in which all of the

(Continued on next page)

suggestions may be subject to careful examination, and that the enactment of a program be the first order of business of the committee in January."

TRADE NAME PRESCRIBING DEFENDED AT HEARINGS

A prominent pharmacist strongly defended the use of trade name prescribing of drugs by physicians in testimony before the Senate antitrust subcommittee studying drug pricing practices.

Charles O. Wilson, Dean of the School of Pharmacy at Oregon State College, said it would be "extremely shortsighted" for physicians to prescribe solely by generic name due to the differences in potency, absorption rates, and quality standards of many drugs classified under a single generic name.

Sen. Estes Kefauver (D., Tenn.), chairman of the subcommitttee, has repeatedly expressed the idea that generic name prescriptions would save patients money and would make no difference in the quality and efficacy of the drug.

However, Wilson refuted this concept. For example, he said, an aspirin tablet could be manufactured that could be sold for nine cents a hundred tablets, "but it would pass right through you and you would still have your headache."

Wilson urged that some system be set up to achieve a consistency in the nomenclature of generic terms. "We in the practice of pharmacy and medicine should have some control over which generic names and which chemical names are going to be used. . . . There should be designated for each pharmaceutical agent, one official chemical name and one official generic name."

WARNING LABEL GUIDE FOR DRUGS

The Food and Drug Administration has issued a list of label warning statements for the guidance of drug manufacturers who are required by law to provide "such adequate warnings . . . as are necessary for the protection of users."

FDA Deputy Commissioner John L. Harvey noted that with relatively few exceptions the drug manufacturer is responsible for choosing the language of the warning. Exceptions include habit-forming drugs and antibiotics. The guide was published to state what FDA considers to be one way of complying with the law.

The new service should be helpful to any drug firm planning to begin distribution of an over-the-counter drug not previously in its line; should make it easier for all drug firms to review their labels; for them to change those not appearing to meet legal requirements, and avoid possible future litigation, said the FDA.

Typical suggested warnings were as follows: "Don't apply to broken skin"; "Do not exceed recommended dosage"; "Do not drive or operate machinery while taking this medication"; "Discontinue use if rapid pulse, dizziness, or blurring of vision occurs"; and "If pain persists for more than 10 days or redness is present, or in conditions affecting children under 12 years of age, consult a physician immediately."

The report, issued in looseleaf form for any firms or persons desiring it, includes suggested warnings for more than 140 drugs or drug classes, including those for animal use, and several therapeutic devices. Requests for the service, which will be kept up to date on changes, may be made to the Food and Drug Administration, Division of Public Information, Washington 25, D. C.

CANCER INCIDENCE REPORT

The director of the National Cancer Institute reported that stomach cancer has been rapidly decreasing in this country but at the same time there has been a jump in the number of cases of lung cancer.

The director, Dr. James R. Heller, told a House appropriations subcommittee that mortality from stomach cancer as well as its occurrence was decreasing for both men and women. The decrease was more spectacular as it affected men, he said because it had been the greatest cancer killer in men.

The incidence of stomach cancer "has diminished in some areas to the point where it has been difficul for surgeons in some of our studies to find enough stomach cancer cases to run a complete series," Dr Heller testified. He said scientists have been unable to establish the cause for the decrease of the disease.

Offsetting this decrease has been an increase in lung cancer, he noted. Asked whether be believed excessive cigarette smoking increased the likelihood of lung cancer, Dr. Heller said he believed that thi was one of the causes. He added that he did no think there was any doubt that air pollution also played a role.

As for all types of cancer, Dr. Heller said the over-all national incidence was increasing and the mortality slightly decreasing.

Some time in the future drugs may be able to cure all cancers, he predicted.

MISCELLANY

The Food and Drug Administration announced a program for the reporting of unusual or adverse reactions to drugs. A limited number of hospitals, selected to represent a cross section of modern specialties, will conduct the study initially. The program is an expansion of a voluntary pilot study carried out during the past four years in cooperation with the American Medical Association, the American Association of Medical Record Librarians, the American Society of Hospital Pharmacists, and the American Hospital Association.

The Public Health Service awarded $1,900,000 for the construction and operation of a monkey research center near Portland, Ore. The funds went to the Medical Research Foundation of Oregon, Inc. Heart Research will be emphasized in the colony of 400 rhesus monkeys.

Mutual of Omaha plans to build an international nursing home and education center in Washington, D. C. Dr. Charles W. Mayo, a member of the insurance firm's board of directors, declared in announcing the project that "free enterprise has taken another step toward showing that the voluntary way can provide a solution to health care problems of the aged."

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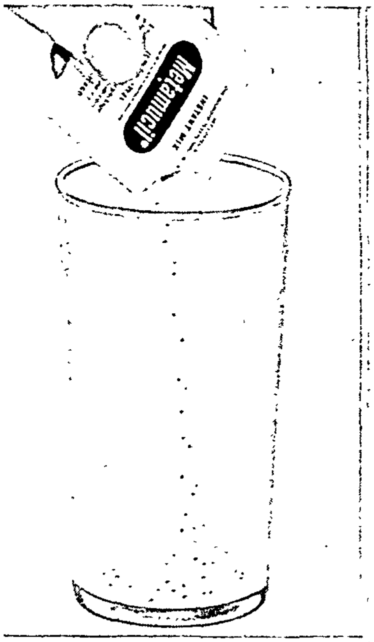

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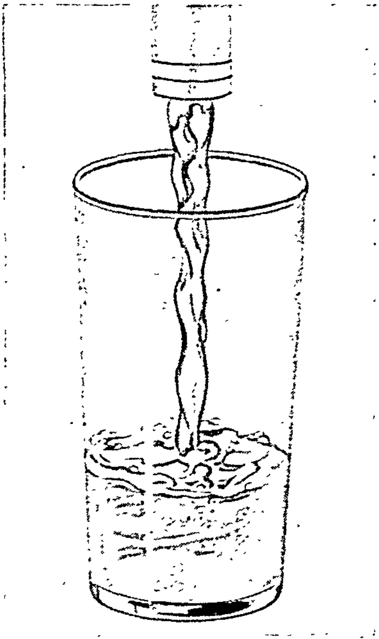

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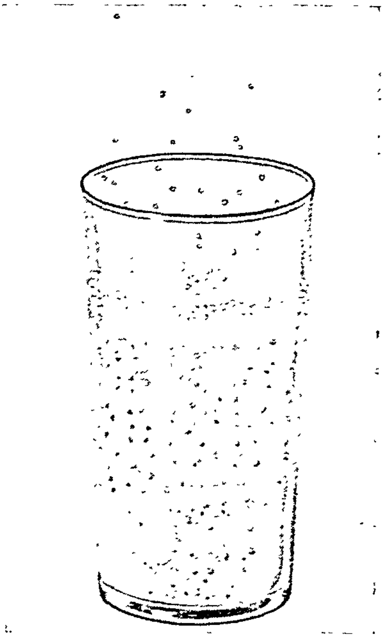

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MEETINGS

AMERICAN MEDICAL ASSOCIATION: Dr. F. J. L. Blasingame, 535 North Dearborn St., Chicago 10, Executive Vice-President.

1960 Annual Meeting, Miami Beach, Fla., June 13-17.
1960 Clinical Meeting, Washington, D. C., Nov. 28-Dec. 1.
1961 Annual Meeting, New York City, June 26-30.
1961 Clinical Meeting, Denver, Nov. 27-30.
1962 Annual Meeting, Chicago, June 11-15.
1962 Clinical Meeting, Los Angeles, Nov. 26-29.

AMERICAN

1960

May

American Association on Mental Deficiency, Lord Baltimore Hotel, Baltimore, May 16-21. Mr. Neil A. Dayton, P. O. Box 51, Mansfield Depot, Conn., Executive Secretary-Treasurer.

American Gynocological Society, Williamsburg Inn, Williamsburg, Va., May 30-June 1. Dr. Andrew A. Marchetti, Georgetown Univ. Hosp., Washington 7, D. C., Secretary.

American Orthopaedic Association, The Homestead, Hot Springs, Va., May 30-June 2. Dr. Lee Ramsay Straub, 535 E. 70 St., New York 21, Secretary.

Illinois State Medical Society, Hotel Sherman, Chicago, May 24-27. Dr. George F. Lull, 185 N. Wabash, Chicago, Secretary.

Minnesota State Medical Association, Kahler Hotel, Rochester, May 23-25. Mr. Harold W. Brunn, 496 Lowry Medical Arts Bldg., St. Paul 2, Executive Secretary.

Symposium on the Psychological and Physiological Aspects of Space Flight, Southwest Research Institute, Hilton Hotel, San Antonio, Texas, May 26-27. For information write Mr. Jack Harmon, 8500 Culebra Rd., San Antonio 6, Tex., Public Relations Director.

June

American Academy of Tuberculosis Physicians, Miami Beach, Fla., June 11. Dr. George P. Bailey, P. O. Box 7011, Denver 6, Secretary.

American Association of Neuropathologists, Statler-Hilton Hotel, Boston, June 11-12. Dr. Leon Roizin, 722 W. 168th St., New York 32, Secretary-Treasurer.

American College of Angiology, Roney Plaza Hotel, Miami Beach, Fla., June 10-12. Alfred Halpern, Ph.D., 11 Hampton Court, Great Neck, N. Y., Executive Secretary.

American College of Chest Physicians, Miami Beach, Fla., June 8-12. Mr. Murray Kornfeld, 112 E. Chestnut St., Chicago 11, Executive Director.

American Diabetes Association, Inc., Hotel Deauville, Miami Beach, Fla., June 11-12. Mr. J. Richard Connelly, 1 E. 45th St., New York 17, Executive Director.

American Electroencephalographic Society, Belmont Hotel, Cape Cod, Mass., June 10-12. Dr. George A. Ulett, 1420 Grattan St., St. Louis 4, Secretary.

American Geriatrics Society, Americana Hotel, Miami Beach, Fla., June 9-10. Dr. Richard J. Kraemer, 2907 Post Road, Warwick, R. I., Secretary.

American Medical Women's Association, Hotel Carillon, Miami Beach, Fla., June 9-12. Mrs. Lillian T. Majally, 1790 Broadway, New York 19, Executive Secretary.

American Neurological Association, Hotel Statler, Boston, June 13-15. Dr. Melvin D. Yahr, 710 W. 168th St., New York 32, Secretary.

American Physical Therapy Association, Penn-Sheraton Hotel, Pittsburgh, June 26-July 2. Miss Lucy Blair, 1790 Broadway, New York 19, Acting Executive Director.

American Physicians Art Association, Miami, June. Dr. Kurt F. Falkson, 7. E. 78th St., New York 21, Secretary.

American Rheumatism Association, Hotel Diplomat, Hollywood-by-the-Sea, Fla., June. Mr. Gerard W. Speyer, 10 Columbus Circle, New York City, Executive Secretary.

American Society of X-Ray Technicians, Netherland Hilton Hotel, Cincinnati, June 11-16. Genevieve J. Eilert, R.T., 16 Fourteenth St., Fond du Lac, Wis., Executive Secretary.

American Therapeutic Society, Barcelona Hotel, Miami Beach, Fla., June 9-12. Dr. Oscar B. Hunter Jr., 915 19th St., N. W., Washington 6, D. C., Secretary.

Association for Research in Ophthalmology, Inc., Miami, Fla., June 12-17. Dr. Lorand V. Johnson, 10515 Carnegie Ave., Cleveland 6, Secretary-Treasurer.

Endocrine Society, Eden Roc Hotel, Miami Beach, Fla., June 9-11. Dr. Henry H. Turner, 1200 N. Walker, Oklahoma City, Okla., Executive Secretary.

Idaho State Medical Association, Sun Valley, June 15-18. Mr. Armand L. Bird, Sonna Bldg., Boise, Idaho, Executive Secretary.

Maine Medical Association, Hotel Samoset, Rockland, June 19-21. Dr. Daniel F. Hanley, P. O. Box 240, Brunswick, Maine, Executive Director.

Northwest Proctologic Society, Roche Harbor, San Juan Island, Wash., June 21-24. Dr. L. D. Leslie, 1162 Willamette St., Eugene, Ore., Secretary-Treasurer.

Society of Biological Psychiatry, Deauville Hotel, Miami Beach, Fla., June 11-12. Dr. George N. Thompson, 2010 Wilshire Blvd., Los Angeles 57, Executive Secretary.

Society for Investigative Dermatology, Inc., di Lido Hotel, M Beach, Fla., June 13-15. Dr. Herman Beerman, 255 S. 17th St., delphia 3, Secretary-Treasurer.

Society of Nuclear Medicine, Estes Park, Colo., June 22-25. Dr. P. Sears, Veterans Administration Hospital, Denver 20, Chairman.

Society for Vascular Surgery, di Lido Hotel, Miami Beach, Fla., 12. Dr. George H. Yeager, 314 Medical Arts Bldg., Baltimore 1, retary.

July

American Goiter Association, Church House, London, England, 5-8. Dr. John C. McClintock, 702 Madison Ave., Albany 8, N. Secretary.

American Society of Facial Plastic Surgery, Hotel Elysee, New City, July 22. Dr. Samuel M. Bloom, 123 E. 83d St., New York Secretary.

Flying Physicians Association Hawaii Cruise, leaving Los Angeles San Francisco, July 11. For information write Mr. Mark E. P. O. Box 3275, Tulsa, Okla.

Oregon Cancer Conference (Second Annual), Sheraton Hotel, land, July 7-8. Dr. Martin A. Howard, 115 S. W. Taylor St., Port 5, Ore., Chairman.

Rocky Mountain Cancer Conference, Hilton Hotel, Denver, July Mr. Harvey T. Sethman, 835 Republic Bldg., Denver 2, Executive retary, Colorado State Medical Society.

August

American Association of Blood Banks, Jack Tar Hotel, San Fra Aug. 21-26. For information write: AABB Central Office, Suite 30 N. Michigan, Chicago 2.

American Congress of Physical Medicine and Rehabilitation, flower Hotel, Washington, D. C., Aug. 21-26. Mrs. Dorothea C. Au 30 N. Michigan Ave, Chicago 2, Executive Secretary.

American Hospital Association, Civic Auditorium, San Francisco, 27-Sept. 1. Mr. Maurice J. Norby, 18 E. Division St., Chicago, Director.

American Institute of Ultrasonics in Medicine, Statler-Hilton Washington, D. C., Aug. 20. Dr. Dorothy M. Stillwell, Dept. of Med. and Rehab., Univ. of Colorado Med. Center, Denver 20, Cha

American Physiological Society, *Stanford University, Calif.*, Au 26. Mr. Ray G. Daggs, 9650 Wisconsin Ave., Washington 14, Executive Secretary.

American Society of Clinical Hypnosis, Miami, Fla., Aug. 7- Seymour Hershman, 6770 N. Lincoln Ave., Chicago 46, Secreta

American Veterinary Medical Association, Denver-Hilton Hote ver, Aug. 15-18. H. E. Kingman Jr., 600 S. Michigan Avenue, 5, Executive Secretary.

Biological Photographic Association, Inc., Utah Motor Lod Lake City, Utah, Aug. 23-26. Miss Jane H. Waters, Box 1668, Central P. O., New York 17, Executive Secretary.

Conference on the Chemical Organization of Cells: Norm Abnormal, University of Wisconsin, Madison, Aug. 25-27. Dr. McManus, Dept. of Pathology, University of Alabama Medical Birmingham, Chairman.

Gerontological Society, Inc., Mark Hopkins Hotel, San Francis 7-12. Mrs. Marjorie Adler, 660 S. Kingshighway Blvd., St. L Administrative Secretary.

National Medical Association, Inc., Penn-Sheraton Hotel, Pit Aug. 8-11. Dr. John T. Givens, 1108 Church St., Norfolk, Va., tive Secretary.

Reno Surgical Society, Mapes Hotel, Reno, Nev, Aug. 18-20. bert G. Lenz, 505 S. Arlington Ave., Reno, Nevada.

Rocky Mountain Radiological Society, Denver-Hilton Hotel, Aug. 11-13. Dr. John H. Freed, 4200 E. 9th Ave., Denver 20, S Treasurer.

St. Joseph's Hospital Annual Clinics, St. Joseph's Hospital, Aug. 3-5. Dr. W. H. Leitch, St. Joseph's Hospital, 1818 Humb Denver 18, Chairman.

West Virginia State Medical Association, The Greenbrier Sulphur Springs, Aug. 25-27. Mr. Charles Lively, Box 1031, C 24, W. Va., Executive Secretary.

September

American Medical Writers' Association, Hotel Morrison, Sept. 30-Oct. 1. Dr. Harold Swanberg, 510 Maine St., Qui Secretary.

American Roentgen Ray Society, Ambassador Hotel, Atlan Sept. 27-30. Mr. Hugh Jones, 20 N. Wacker Dr., Chicago 6, Public Relations.

American Society of Clinical Pathologists, Palmer House, Sept. 24-Oct. 2. Mr. Claude E. Wells, 445 Lake Shore Drive, 11, Executive Secretary.

College of American Pathologists, Palmer House, Chicago, S 27. Dr. Arthur H. Dearing, 2115 Prudential Plaza, Chicago, E Director.

Colorado State Medical Society, Stanley Hotel, Estes Park, S 17. Mr. Harvey T. Sethman, 835 Republic Bldg., Denver 2, E Secretary.

Delaware, Medical Society of, Rehoboth, Del., Sept. Mr. L C. Morris Jr., 1925 Lovering Ave., Wilmington 6, Del., E Secretary.

Flying Physicians Association, third clinical meeting, West Lodge, Wagoner, Okla., Sept. 6-9. For information write: Flyin cians Association National Headquarters, P. O. Box 3275, Tul

(Continued on page 32)

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ROLE OF FIBRINOLYTIC AGENTS IN THROMBOTIC DISEASES

R. V. Chapple, M.D.
and
H. O. Singher, Ph.D., Raritan, N. J.

Critical analysis of existing data demonstrates that fibrinolysin in conjunction with anticoagulant therapy decreases the morbidity in patients with thrombophlebitis. This conclusion was the result of comparison of data from hospital charts of 20 patients in a fibrinolysin-treated series and a control group of 22 patients. The comparison was made after outlining the necessary criteria for the arbitrary selection of patients and setting up rules to be followed in the interpretation and grading of the clinical information. The author also reviews the theories of clot lysis that have been put forward, with the realization that a final answer has not yet been determined.

THE changing concepts of the physiological role of fibrinolytic systems in the body has highlighted a complex enzymatic system, which may possibly have wide implications in the therapy of disease. Numerous investigators[1] have reported the spontaneous occurrence of a low order of fibrinolytic activity in normal persons. The nature of this activity, as well as the mechanism whereby its action becomes apparent, is of some significance in relation to the therapeutic use of this system.

While these concepts have been changing, they have all dealt with resultant enzymatic activity; either being present in the circulating plasma, being adsorbed on a fibrin clot, or created within a clot. Several mechanisms have been proposed to explain these activities. The classic mechanism indicated that the enzyme in its active form was circulating in plasma. It was then preferentially adsorbed to the clot. More recently, Sherry and co-workers[2] have introduced a new concept of this activity. They have differentiated between fibrinolytic activity and thrombolytic activity. They have defined fibrinolytic activity as the action of the enzyme. Thrombolytic activity results from the action of the activator on proenzyme adsorbed to the clot. Thus, in their hypothesis only an enzyme produced *de novo* in the clot is effective in producing clot dissolution.

Ambrus and co-workers[3] have introduced another approach to the concept of relative affinities of inhibitors and clot for the enzyme. These investigators believe that there is evidence for the selective adsorption of the enzyme to a fibrin clot. They indicate that, when an enzyme is combined with circulating inhibitor, the clot has a greater affinity for the enzyme than does the inhibitor. As a result, the clot can dissociate the combination and selectively adsorb the enzyme.

Presented at the World Conference of Angiology, Atlantic City, June 5-7, 1959.

Second, patients selected as control cases were those in whom the pertinent history was similar to that of the patients in the fibrinolysin-treated group and in whom the daily record notes were adequate.

Third, patients were classified as severe or mild cases, depending on whether two of the three main features, pain, tenderness, and swelling were so designated. The condition of those patients in whom the degree of pain, tenderness, and swelling was not specified, was classified as "degree not specified."

TABLE 2.—*Clinical Data on Patients with Deep Thrombophlebitis*

		Fibrinolysin-treated Group, No.	Control Group, No.
Varicose veins		3	3
Previous phlebitis		1	3
Pulmonary emboli associated with		2	5
	Pregnancy	5	1
	Operation	1	3
	Leg trauma	2	2
	Medical illness	4	4
Prothrombin time, sec	14-18	1	2
	19-22	4	4
	23-30	8	7
	31-40	1	3
	No data	6	6

Fourth, the end-point for definitive changes in morbidity was taken to be the number of days from the start of fibrinolysin or anticoagulant administration to the first day in which swelling or discomfort was absent.

Fifth, data in those patients with discomfort or swelling still present on discharge from the hospital were not included in the calculation of results.

Sixth, extremity measurements showing differences in circumference between

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As shown in table 2, the present attack was ass ciated with pregnancy in five patients in the fib nolysin-treated group as compared to one patie in the control group. The history of thromboemb lic disease was about the same in both series. Th available laboratory data showed that patients both groups had reached satisfactory prothromb levels during treatment.

Results

Table 3 shows the relative effects of treatment discomfort and swelling with anticoagulants in t control patients and with fibrinolysin in the 10 p

incidence of the anticoagulant administration a

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various fibrinolytic agents on experimental thrombi in animals.

Warren and Villavicencio [9] have demonstrated the actual lysis with fibrinolysin of a normal clot in the femoral vein of a dog. Lysis in their series was induced in 11 to 27 minutes.

Johnson's and McCarty's [5] studies on experimental clots in man demonstrated the validity of animal data for at least one agent in the human being.

The difficulties in precise diagnosis, etiology, and pathology of venous thrombosis have been well documented.[10] Similarly, the difficulty in following the response to any therapy is due to the limitation of specific diagnostic methods. In order to overcome these limitations, two pathways are open, namely, (1) use of venograms before and after therapy in patients with clinical evidence of thrombophlebitis to demonstrate the re-establishment of circulation, and (2) critical analysis of a control study of alternate patients demonstrating similar clinical histories and findings.

Venography has been used by Evans and Smedal [11] and Sokal and co-workers,[12] showing the clearance of a filling defect after fibrinolysin therapy.

bolism also continues to be the most common lung disorder in spite of anticoagulant therapy.

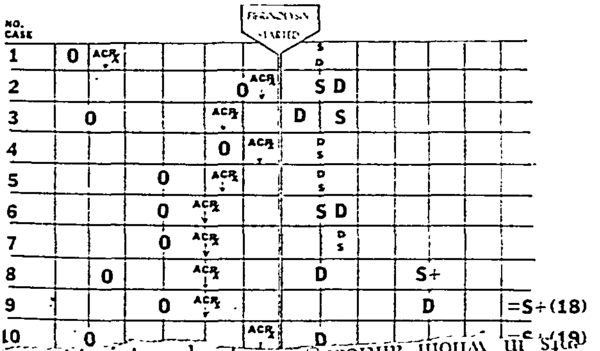
Two thrombotic diseases, thrombophlebitis and pulmonary embolism, have been studied extensively with use of fibrinolysin (human) (Actase) in conjunction with standard forms of therapy. Although it has been reported, without confirmation, that a difference exists in the effectiveness of different fibrinolytic materials, the unsettled state of the theoretical basis of activity precludes interpretation on levels other than clinical measurements. This situation is analogous to that in the use of many important drugs. The therapeutic response to administration of penicillin is well known, while its mechanism of action remains, even at this late date, unknown.

Clinical Effects

The clinical effects of fibrinolysin have been studied in 400 patients with a variety of circulatory disorders. With the exception of persons with coronary disease, these include studies of patients with a diagnosis of cerebral thrombosis, cerebral emboli, thrombotic and embolic disease of the peripheral and splanchnic arterial system, pulmonary embolism, and venous thrombosis. Most of the patients showed no changes in the components to nine days before the first fibrinolysin infusion. The results of treatment are shown to the right of the heavy vertical line as time in days for the disappearance of discomfort and swelling after the start of fibrinolysin treatment. In cases one through seven, both discomfort and swelling were found to have disappeared by the third day after the start of treatment with fibrinolysin. This was true irrespective of the time of the onset of the attack and the day on which anticoagulant treatment was started. Likewise, in cases 8 and 10, discomfort disappeared within this interval. Discomfort was found to disappear within eight days in case 8.

Pulmonary Embolism

No satisfactory, definitive method of accurate diagnosis of pulmonary embolism exists, nor are there adequate procedures for assessing the effectiveness of therapy. The usual criteria are the rapidity of resolution of roentgenographic findings,



variable intervals of improvement. Since these are unselected cases, it must be realized that these figures represent patients with organized thrombi, in whom we would not anticipate any response.

The data were then reviewed with respect to the age of the thrombus and the response to fibrinolysin therapy. This is a difficult point to determine, since patients' histories are sometimes clinically inaccurate. However, the error is assumed constant for all. Here again, if data were not available the case was eliminated from the study. In view of the usual organization or epithelization, or both, of a clot within a five-day to seven-day period, it was decided to assess response by the previously mentioned criteria in the clots aged under five and over five days. Eighty-three per cent of the group with a thrombus under five days of age fell within the response criteria outlined previously. Only 62% had the indicated response if the clot was over five days old.

While one might theoretically anticipate an increased incidence of embolization in such lytic type of therapy, this has not proved to be the case. Actually, 3 in a series of 171 patients with thrombophlebitis have developed clinical symptoms of pulmonary embolism. No untoward sequelae were observed. It is believed that the presence and

Summary

While many theories of clot lysis have been put forward, insufficient data are available to achieve a final decision at this time. Critical analysis of existing data demonstrates that fibrinolysin (human) (Actase) in conjunction with anticoagulant therapy decreases the morbidity in patients with thrombophlebitis. While a decrease in morbidity from pulmonary embolism is observed, more exact methods of diagnosis and criteria of effectiveness are required.

While the case reports of many evaluators were reviewed, the assessment and conclusions are those of the authors.

Dr. W. P. Chapman, of the Boston Globe, Boston, acted as the independent evaluator of the data submitted.

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Response to anticoagulant therapy,

Range	<7-14	
Severity of symptoms, days		
Marked	13	6
Degree not specified	6	15
Mild	1	1

treated patients also received anticoagulants. In 10 patients, the administration of anticoagulants (heparin, then bishydroxycoumarin [Dicumarol]) and fibrinolysin was started on the same day. In the others, fibrinolysin was first given from one to nine days after the start of anticoagulant therapy. An important reason for initiating fibrinolysin treatment in certain patients who had already received anticoagulant therapy was that there had been little or no improvement in their clinical course.

Criteria

The criteria used in the arbitrary selection of the fibrinolysin-treated patients and controls and the rules followed in the interpretation and grading of the clinical data for this report on morbidity are as follows:

First, all patients selected were those in whom the history and case record notes were satisfactory for the daily appraisal of the main features of the acute disease, namely, discomfort, which included pain or tenderness, or both, and limb swelling.

Second, patients selected as control cases were those in whom the pertinent history was similar to that of the patients in the fibrinolysin-treated group and in whom the daily record notes were adequate.

Third, patients were classified as severe or mild cases, depending on whether two of the three main features, pain, tenderness, and swelling were so designated. The condition of those patients in whom the degree of pain, tenderness, and swelling was not specified, was classified as "degree not specified."

TABLE 2.—*Clinical Data on Patients with Deep Thrombophlebitis*

		Fibrinolysin-treated Group, No.	Control Group, No.
Varicose veins		3	3
Previous phlebitis		4	3
Pulmonary emboli associated with		3	5
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	19-22	4	4
	23-30	8	7
	31-40	1	3
	No data	6	6

Fourth, the end-point for definitive changes in morbidity was taken to be the number of days from the start of fibrinolysin or anticoagulant administration to the first day in which swelling or discomfort was absent.

Fifth, data in those patients with discomfort or swelling still present on discharge from the hospital were not included in the calculation of results.

Sixth, extremity measurements showing differences in circumference between the two lower extremities of less than 2 cm. were regarded as not significant.

Seventh, discomfort or swelling described as estionable or minimal was regarded as within ormal range.

Eighth, if a progress note, which stated that discomfort or swelling was absent, did not make clear the date on which the disappearance occurred, the date indicating the absence of discomfort or of swelling was arbitrarily taken to be the day after the previous date in the record which noted these abnormalities to be present. (Gaps in the daily note record presented some difficulties in the assessment of changes in morbidity. In the control series there were three patients in whom there was a four-day gap and one patient in whom there was a seven-day gap, between the last daily note in the record indicating the presence of discomfort, or swelling, or both, and the first day on which they were noted to be absent. In determining the duration of morbidity it might have been preferable to have indicated the time of disappearance of swelling or discomfort by subtracting one day from the first day on which the note indicated their disappearance. This device was not used, since it would have increased the spread between the mean values for the disappearance of discomfort, or swelling, or both, in the two series.)

Ninth, all except four patients from both groups were examined, and their conditions were evaluated by the same physician.

Tenth, this report represents an independent evaluation by another physician of the reported data in all patients.

The pertinent data on the history and status of the patients with thrombophlebitis in both groups are shown in tables 1 and 2.

There were 20 patients in the fibrinolysin-treated series and 22 patients in the control series (table 1). The control patients were nearly seven years older on an average and had nearly the same age range and an average duration of the present attack that was three days less than that of those in the fibrinolysin-treated group. In the fibrinolysin-treated series, the thrombophlebitis was described as severe in 13 patients as compared to 6 patients in the control group.

As shown in table 2, the present attack was associated with pregnancy in five patients in the fibrinolysin-treated group as compared to one patient in the control group. The history of thromboembolic disease was about the same in both series. The available laboratory data showed that patients in both groups had reached satisfactory prothrombin levels during treatment.

Results

Table 3 shows the relative effects of treatment of discomfort and swelling with anticoagulants in the control patients and with fibrinolysin in the 10 pa- [illegible] anticoagulant administration and fibrinolysin infusion were both started on the same day. In the fibrinolysin-treated group, discomfort was found to disappear in an average of 2.8 days, with a range of from 1.0 to 5.0 days. Swelling disappeared in an average of 2.0 days, with a range of from 1 to 4 days. In contrast, discomfort disappeared in 19 control patients in an average of 6.0 days, with a range of from 2.0 to 14.0 days, and swelling disappeared in 18 control patients in an average of 5.2 days, with a range of from 2.0 to 10.0 days. The 10 patients in the fibrinolysin-treated group were similar to the control patients with respect to average age, age range, duration of present attack before treatment, severity of the thrombophlebitis, and relative incidence of calf only and calf-plus-thigh involvement.

TABLE 3.—*Comparison of Days* of Treatment to Absence of Discomfort and Swelling*

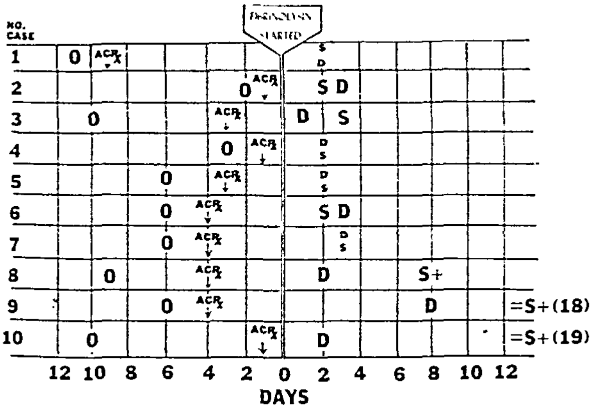
	Fibrinolysin-treated Group† Days			Control Group Days		
	Cases, No.	Average	Range	Cases, No.	Average	Range
Discomfort absent	10	2.8	1-5	19	6.0	2-14
Swelling absent	10	2.0	1-4	18	5.2	2-10

* From start of therapy.
† Fibrinolysin and anticoagulant therapy started on same day.

The figure shows the effects on discomfort and swelling in the 10 fibrinolysin-treated patients in whom anticoagulants were administered from one to nine days before the first fibrinolysin infusion. The results of treatment are shown to the right of the heavy vertical line as time in days for the disappearance of discomfort and swelling after the start of fibrinolysin treatment. In cases one through seven, both discomfort and swelling were found to have disappeared by the third day after the start of treatment with fibrinolysin. This was true irrespective of the time of the onset of the attack and the day on which anticoagulant treatment was started. Likewise, in cases 8 and 10, discomfort disappeared within this interval. Discomfort was found to disappear within eight days in case 8.

Pulmonary Embolism

No satisfactory, definitive method of accurate diagnosis of pulmonary embolism exists, nor are there adequate procedures for assessing the effectiveness of therapy. The usual criteria are the rapidity of resolution of roentgenographic findings, when present, and the reversal of clinical symptoms and the infrequency of recurrence. The recent work of Robin and co-workers [15] in measuring arterial and end-tidal carbon dioxide tension may provide a useful clinical research tool in this disease.



Number of days between initial administration of fibrinolysin and onset of attack and initial administration of anticoagulant therapy and disappearance of pain and swelling. Time of first fibrinolysin infusion is indicated by vertical line in center of chart; this time is indicated as "zero" day. *O*, shows onset of attack; *D*, indicates absence of discomfort; *S+* reveals presence of swelling; ACR$_x$, indicates start of anticoagulant therapy; *S*, shows absence of swelling.

At present, more experience in the use of the fibrinolysin preparation has resulted in patients' more rapid recovery from pulmonary embolism. This has occurred without sequelae. The same interval of clot age in relation to therapeutic response as in the thrombophlebitis data is present. There is an apparent decrease in recurrence rate.

It is recognized that intravascular thrombotic episodes are not confined to the venous tree or to the pulmonary system. Clinical investigations of thrombotic incidents in the arterial circulation are proceeding.

Summary

While many theories of clot lysis have been put forward, insufficient data are available to achieve a final decision at this time. Critical analysis of existing data demonstrates that fibrinolysin (human) (Actase) in conjunction with anticoagulant therapy decreases the morbidity in patients with thrombophlebitis. While a decrease in morbidity from pulmonary embolism is observed, more exact methods of diagnosis and criteria of effectiveness are required.

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OBSERVATIONS ON FECAL CONTINENCE MECHANISMS

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and
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Fecal continence depends on the integrity of three intestinal functions. One is the reduction of bulk by water absorption; another is the retention of fecal substance by reservoir action in certain parts of the colon; the third is the action of sphincters. Sphincteric continence is not merely a "purse-string" phenomenon but represents a more complex anorectal reflex. The receptor areas in the rectum were for many years considered to be in the mucosa; it is more likely that they are in the rectal musculature. Other assumptions about the physiology of continence mechanisms must similarly be revised. There is evidence that hitherto unexplained adaptive mechanisms enable the body to compensate for the surgical removal of some functional units.

The function of the fecal continence mechanisms interested many early physiologists and anatomists. However, they frequently presumed that function can be implied directly from known anatomic structure. This, probably, is responsible for several misconceptions which originated at that time and persist today. The mechanisms of defecation and continence must be differentiated. By definition, defecation involves the elimination of the contents of the gastrointestinal tract but does not concern itself with the form or timing of elimination. All control of the bowel, other than direct expulsion, is a function of continence rather than of defecation. The following discussion will be confined exclusively to the consideration of factors affecting fecal continence.

Many standard physiological and surgical textbooks discuss the defecation mechanisms in detail but ignore almost completely any reference to continence. A careful search of the literature has revealed no publication correlating experimental findings with clinical observations. However, recent investigations have brought to light several interesting facts. We have been able to correlate these with our own observations made during experimental studies on eradication of abnormal rectal mucosa.

Mechanisms

Functional Bowel Units.—Continence depends to a large extent on the conversion of the liquid voluminous small bowel contents into a semisolid material, of considerably decreased bulk, which can be conveniently stored until evacuation is opportune. To accomplish this, the bowel is divided into several functional units. The increase in viscosity and reduction in volume of the bowel contents are accomplished by a high rate of water absorption in the terminal ileum and ascending colon and by bacterial growth. Both of these phenomena depend on a relatively slow movement of the fecal stream in this segment of bowel. The descending colon is primarily concerned with the storage of the products it receives, until periodically stimulated to initiate evacuation. The third functional unit comprises the rectum and anal sphincters, which are intimately interrelated in their action. Gaston[1] concluded, after investigation, that the reflex control of this latter unit is accomplished by receptors in the rectum which transmit stimuli through the parasympathetic nervous system to subcortical and cortical centers. The activity of these receptors was noted to decrease progressively from the distal to the proximal part of the rectum and was entirely absent in the sigmoid colon. The motor limb of this reflex arc is transmitted via the somatic tracts, through the hemorrhoidal nerves, to the external anal sphincter.

Reservoir and Sphincteric Continence.—On the basis of studies with pressure-measuring balloons, Gaston[1] subdivided the mechanisms of fecal continence into reservoir and sphincteric elements.

To act as a reservoir organ, the descending part of the colon adapts itself to the changing bulk of its contents. When a mass of certain critical volume is accumulated, or when stimulated by various reflexes (e. g., gastrocolic), this portion of the bowel propels the colonic contents into the rectum. This usually occurs as a unit evacuation of the entire descending colon, which has been termed the "colonic rush." There is some doubt whether this "unit expulsion" occurs only during defecation or whether it may operate from time to time only to be insensibly inhibited by various reflex mechanisms. The reservoir function of continence is well illustrated in patients with sigmoid colostomies, who with proper care develop a certain degree of control of solid material.

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Sphincteric continence is not merely a "purse-string" phenomenon but represents a more complex anorectal reflex. The internal anal sphincter plays no part in the continence mechanism, for, as Gaston showed, it relaxes as soon as the rectum is distended. This operates via a reflex mediated in the spinal cord,[2] and, indeed, the cutting of the internal sphincter produces no disability at all.[3] Therefore, any further references in this paper to the anal sphincter should be considered to include only the external sphincter.

Feces, on entering the rectum, produce the familiar lower pelvic sensation and stimulate an expulsive peristaltic wave which reaches its peak in a few seconds and quickly subsides. At the same time, the anorectal reflex previously described stimulates the external sphincter to contract beyond its normal tone and resist the expulsive forces. These contractions soon diminish (within 50 or 60 seconds) because of muscle fatigue. However, they persist well beyond the period when rectal peristalsis subsides, and therefore continence is preserved. Central inhibition of this reflex allows defecation at the appropriate time.

The receptor areas in the rectum were for many years considered to be in the mucosa, since it was noted that local anesthetic agents eliminated the ability of the patient to differentiate between solids, liquids, and gases and impaired their continence.[4] However, the present understanding that these agents also have a direct paralytic effect on smooth muscle throws doubt on this concept. Karlan and co-workers [5] showed, in studies with dogs, that complete removal of the rectal mucosa followed by an anastomosis of the terminal ileum to the remaining muscular tube of rectum does not interfere with this reflex. Further confirmation of their results was derived from our experiments with use of similar preparations. These authors have also shown that, in dogs, complete resection of the rectum and colon followed by ileoanal anastomosis destroys the anorectal reflex and disturbs continence to such an extent that these animals all die of progressive inanition. Therefore, one can assume that the receptor areas are located in the rectal musculature. The terms "contraction receptors" or "pressure receptors" are more accurate than the now commonly used term "stretch receptors," because it is well known that the bowel is insensitive to simple stretch, as evidenced by the plastic adaptation of the large bowel to the fecal contents. It is only when an increased intraluminal pressure, produced by muscular contraction, occurs that some receptor area is activated and made aware of the bowel contents.

The mechanism of differentiation between solids and gases is uncertain. It may be related to the differences in pressure exerted by these agents within the rectum.[3] Liquids are poorly distinguished from solids and gases until contact is made with the anal skin.

Clinical Correlation

Gaston [1] has suggested that cases of total resection of the rectum offer clinical proof of the nature of the anorectal reflex. He described a patient who had a total proctectomy with a sigmoid-anal anastomosis. Although this patient could actively constrict her anus at will, she was unaware of the proper time to do so and thus really had no more than a perineal colostomy with a functionally ineffective sphincter. Similarly, this explains how an elderly person, whose measured voluntary anal contractile force is low, retains his continence by corresponding decrease in his rectal expulsive powers.

In contradiction to Gaston's concepts are the results obtained in the currently popular sphincter-preserving procedures for carcinoma of the midsection of the rectum. Many authors[6] report a high percentage of normal continence after removal of the entire rectum, with or without anal skin, followed by anastomosis of the sigmoid colon to the anus. Up to 75% of these patients in a large series[6a] were claimed to have retained the urge to defecate with functional sphincter control. Similarly, section of the parasympathetic nerves, as reported by Schlitt and co-workers [7] and others for the treatment of ulcerative colitis, does not seem to interfere with continence. Indeed, in these cases continence is improved by the decrease in bowel motility. It appears, therefore, that the anorectal reflex does not fully warrant the significance attributed to it, or else it is qualitatively replaceable. A third possibility might be that the receptor area is not always entirely removed by total resection of the rectum.

Attempts have been made to determine the minimum amount of reservoir organ required to maintain normal function and the minimum amount of residual rectum necessary to preserve the anorectal reflex. Both of these probably vary with the segment involved, necessitating greater length the more proximal the segment preserved. Goligher[8] reviewed 171 patients who had undergone various operative procedures; he found that in those patients who had 7 to 8 cm. of distal rectum retained, satisfactory continence invariably resulted. When only 6 cm. of rectum was preserved, about 80% had favorable results. Perhaps the failures were due to nerve damage caused by inversion of the rectal stump for a pull-through procedure which was used for anastomosis with these shorter rectal segments. In proximal rectosigmoidectomy for prolapse, in which only 1.75 cm. of rectal remnant was left, only 50% of the patients retained what was described as fair continence, and in the other half results were poor. These patients, of course, originally had poor rectal tone.

Ileoproctostomy invariably gave good results, but the ileoanostomy described by Ravitch[8] is reported to give variable results by various investigators. Ravitch's procedure consisted essentially of total colectomy followed by dissection of the rectal mucosa and submucosa from the muscularis. The terminal ileum was then brought through the lumen of the muscular rectal wall to be anastomosed to the anus. Ravitch[8] has performed this procedure in many cases to date and reports excellent results in patients with multiple polyposis but indifferent results in cases of idiopathic ulcerative colitis. He attributes the latter poor results to several factors, including the emotional make-up of these patients, their debilitated condition at the time of surgery, and the results of many previous infective episodes involving the bowel wall. Ravitch's work has received relatively little support on this continent[8] and in England,[9] after trial by various groups. However, many surgeons in continental Europe and elsewhere[10] described excellent results with this technique. Of course, in all procedures in which large or critical areas of the bowel are removed, a period of adjustment is required before continence returns. The adjustment period after Ravitch's ileoanostomy is particularly trying, and this may be one of the reasons why many surgeons dislike this procedure.

Although it is fairly well established that the terminal 30 cm. of ileum may assume most of the water-absorptive function of the excised colon, it is a matter of conjecture whether the ileum will function as a reservoir organ in the absence of large bowel. Those who claim satisfactory results with Ravitch's procedure and its resulting dilatation of the small bowel must believe that ileum will indeed substitute for colon. Swenson[11] reported that, in children with Hirschsprung's disease involving the entire colon and part of the terminal ileum, a total colectomy and rectosigmoidectomy followed by "a pull-through type of anastomosis, such as used in the common form of congenital megacolon" is the treatment of choice. After a time, "growth and development become normal" in these patients. Swenson[11] did not discuss the degree of continence achieved but stated only that his series of five patients "have done well." By his description, these patients are left with 2 or 3 cm. of rectum, which should be a considerable proportion of the child's rectum. The young age of these patients may also explain why results are better than might be expected in adults.

Various techniques have been devised to construct a reservoir from the small bowel. Valiente and Bacon[12] experimented on dogs, with a "pantaloon technique" of side-to-side anastomosis of an S-shaped segment of terminal ileum, interposed between the anus and the small bowel. Their results were equivocal. Gilbertas and Blanchard[13] constructed a pouch from a loop of ileum with a side-to-side anastomosis, with fair results in one patient. Karlan and co-workers[5] repeated Valiente and Bacon's experiment but left a 4-cm. segment of rectum denuded of mucosa. They found that this functioned poorly. A side-to-side pouch of isoperistaltically aligned ileum gave excellent results in dogs if the rectal cuff was preserved. However, when attempted on one patient, results were equivocal.

Conclusions.—The foregoing is a discussion of most of our present knowledge about the fecal continence mechanism and indicates many problems which remain to be solved. Gaston's observations on continence appear to be valid for physiological situations; however, what is yet uncertain is the extent to which the body is able to adjust to or substitute for these mechanisms in pathological or abnormal conditions. Much investigation has yet to be carried out into the nature of the anorectal reflex and the reservoir component of fecal continence. More data are necessary before we will be able to ascertain which surgical procedures would best facilitate removal of any diseased bowel and still preserve the important continence function.

Summary

The bowel may be subdivided into three functional units with regard to continence. The first is the terminal ileum and ascending colon, in which considerable water absorption is carried out. The descending colon is primarily a storage organ. The rectum and external sphincter are interrelated by reflexes mediated in cortical and subcortical regions functioning to preserve continence until elimination is opportune.

Under physiological conditions the continence mechanism can be divided into reservoir and sphincteric components. The sphincteric component involves the reflex interaction of the rectum and external sphincter. Adaptation factors, which are responsible for apparently normal function after surgical removal of these functional units, are as yet unexplained.

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EARLY DIAGNOSIS OF CONGENITAL DYSPLASIA AND CONGENITAL DISLOCATION OF THE HIP

VALUE OF THE ABDUCTION TEST

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and
John R. Hodgson, M.D., Rochester, Minn.

To appraise the accuracy and possible limitations of the (thigh) abduction test in the diagnosis of congenital hip joint abnormalities the test was specifically used in examining 11,010 infants. All infants were examined during their first day of life, again on the fifth day, and (90% of them) at regular intervals for six years. In children routinely examined the average age at the time of diagnosis was 4 months, with no dislocations being undiscovered prior to the weight-bearing age; in children not routinely examined the average age was 14 months. In most infants full 90-degree abduction is unusual after the neonatal period; during the second through the eighth or ninth month abduction is frequently in the range of 60 to 70 degrees. With dysplasia and dislocation, abduction is usually limited to 45 to 50 degrees. Abduction limited to 60 degrees or less should warrant roentgenographic examination.

The purpose of this communication is to present our experience in the early diagnosis of congenital dysplasia and dislocation of the hip. Inclusion of the abduction test in the routine physical examination of the newborn and older infant, with roentgenographic studies of those infants exhibiting a positive result with the test, has enabled us to reduce materially the age at which the diagnosis of congenital disease of the hip is made. There has seemed to be a universal appeal for early diagnosis of the condition, with agreement that early diagnosis and early treatment are the *sine qua non* of optimum results.

We became interested in the early diagnosis of congenital dysplasia of the hip when we were privileged to hear and talk with Dr. Hart,[1] who was enthusiastic about the possibilities of early diagnosis. We had the opportunity to examine all newborn infants in a community and then follow them in well-child clinics. We hoped that inclusion of the abduction test as part of the routine examination of the

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newborn infant would make possible the diagnosis of all dysplasias and dislocations of the hip at birth. Therefore, beginning Jan. 1, 1949, the abduction test was included and the results recorded in the neonatal examinations. All infants were examined within the first 24 hours of life and again on the 5th day. More than 90% of these infants were then seen at regular intervals in the well-child clinics.

Abduction Test as a Screening Method in the Diagnosis of Congenital Dysplasia of the Hip: Periods of Observation and Results

Period	Observation and Results	Av. Age at Diagnosis, Mo.
Jan. 1, 1945 to Dec. 31, 1948	Of 5,929 newborn infants examined (and 90% examined periodically in well-child clinics), 5 evidenced dislocated hips after weight-bearing age	14
Jan. 1, 1949 to Sept. 30, 1950	Abduction test made part of routine examination of newborn infants; one infant with normal abduction at birth later found to have dislocated hip (September, 1950)	14
Oct. 1, 1950 to Dec. 31, 1955	Abduction test emphasized as part of monthly examination in well-child clinics; no dislocations undiscovered by time of weight-bearing age	..
Jan. 1, 1949 to Dec. 31, 1955	Of 11,010 infants examined (and 90% followed in well-child clinics)	
	12 with congenital dysplasia of the hip and luxation	4
	10 with probable congenital dysplasia	2.9

In order to detect infants who might have dysplasia and who had been born prior to Jan. 1, 1949, physicians examining infants in the well-child clinics were encouraged to include the abduction test as part of the routine examination at all ages up to one year. Within the first year it became evident that (1) a normal result with the abduction test at birth did not exclude the possibility that dysplasia or dislocation might become evident later and (2) the test should be part of the examination of all infants at monthly intervals through at least 12 months of age.

The effectiveness of the routine use of the abduction test as a screening method for detection of acetabular dysplasia and dislocation of the hip is manifested by the data in the table. In 5,929 patients first examined as newborn infants, with 90% of them being examined regularly in the well-child clinics from Jan. 1, 1945, through Dec. 31, 1948, the diagnosis of congenital disease of the hip was not made prior to the weight-bearing age, the average age at diagnosis being 14 months. After institution of the abduction test as part of the routine neonatal examination of 11,010 infants born in the period Jan. 1, 1949, through Dec. 31, 1955, the diagnosis of congenital dislocation of the hip was made in two newborn infants and that of probable congenital dysplasia of the hip without dislocation in three newborn infants. All other infants gave negative results with the abduction test during the neonatal period.

Although encouragement was given to use the abduction test as part of the physical examination of all infants less than 1 year of age, the point was not stressed until one of the infants whose abduction test gave a negative result at birth dislocated one of his hips at the time of weight-bearing. After this experience, use of the test in the routine examinations at the well-child clinics was strongly emphasized, and since that time (October, 1950) all dislocations have been detected prior to the weight-bearing age. By the use of the abduction test and roentgenographic examination, the average age at diagnosis was reduced from 14 months to 4 months for dysplasia with dislocation.

The Abduction Test

The abduction test (fig. 1) is simple to perform but requires intelligent application. We have had no difficulty in interpreting the test in the neonatal period when abduction of 80 to 90 degrees is found without undue pressure or without special effort to achieve "optimum conditions." When the results of the abduction test have been positive, they have been quite definitely so, with abduction difficult beyond 45 to 50 degrees.

Interpretation of the results of the test at the subsequent age levels requires more experience. In most infants, full 90-degree abduction is unusual after the neonatal period, and during the 2nd through the 8th or 9th month abduction is frequently in the range of 60 to 70 degrees. With dysplasia and dislocation, abduction is usually limited to 45 to 50 degrees. Abduction limited to 60 degrees or less should warrant roentgenographic examination. Abduction may be limited because of other conditions, such as arthrogryposis multiplex, moderate to severe spasticity, and coxa plana, and may be unexplained in some instances. However, we believe that the test offers a valuable, simple screen-

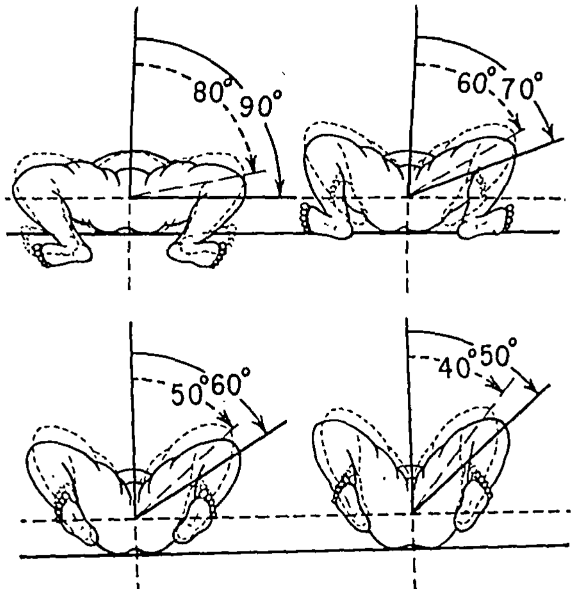

Fig. 1.—Abduction test. Top (*left*), normal at birth to 1 month of age, (*right*) often normal, 1 to 9 months of age. Bottom (*left*), suspected significant limitation, (*right*) definite limitation.

ing procedure for the detection of congenital disease of the hip. The exact mechanism of limitation of abduction in such disease is not fully understood. The limitation that is present in actual dislocation is not difficult to understand, but the limitation that is present when dislocation cannot be demonstrated is of more obscure etiology. Several theories have been suggested but definite evidence to support these theories is lacking.

In our well-child clinics, our experience has been that about two thirds of the infants who had limitation of abduction of a degree considered by the examining physician to warrant roentgenographic examination have had "roentgenographically normal" hips. The infants were examined by pediatricians and pediatric fellows, with varying degrees of experience, in interpretation of the results of the test. The tendency of the less experienced has been to take roentgenograms even when minimal limitation of abduction was shown.

The tendency for greater awareness of the possibility of early diagnosis of congenital dysplasia of the hip by use of the abduction test has led to some confusion. A physician examining an infant may detect what he interprets as limitation of abduction of one or both hips. The infant is referred for roentgenographic examination. Unfortunately, accurate interpretation of the roentgenograms during the neonatal and early-infancy period may be difficult, if not impossible. There has been a surprising lack of knowledge of the normal variations as well as the limitations of the criteria commonly used to diagnose congenital disease of the hip. This was aptly pointed out by Caffey and co-workers.[2]

Undoubtedly, many infants are being treated unnecessarily for questionable or nonexistent "congenital disease of the hip." However, it is also evident that in many instances the diagnosis should be made early but is not, because of failure of detection by clinical examination or because of difficulty in interpretation, or misinterpretation, of the roentgenograms. Children with frank dislocation of the hip which is not discovered until they are 1½ to 2½ years of age are still being referred to the clinic for orthopedic care. All of the infants in our study are now at least 3½ years of age, and in no infant whose progress has been followed with regular examinations has dislocation become evident after weight-bearing age. It would therefore seem that no child with dysplasia and dislocation lacked the clinical signs to permit early diagnosis.

Other Clinical Signs

The other clinical signs that are mentioned in relation to the early diagnosis of congenital dysplasia of the hip are Ortolani's sign (jerk), unequal thigh creases, unequal gluteal creases, unequal length of the legs, external rotation of one leg, and a "clicking" sound on abduction of the hips. Limp is a late sign of congenital dysplasia of the hip.

We have not found Ortolani's sign (jerk of entry and jerk of exit, or either) to be a consistently dependable diagnostic sign. Hart[1] stated that this sign is pathognomonic of dysplasia. We have not infrequently observed infants in whom both the "jerk of entry" and the "jerk of exit" were present within the first 24 hours after birth and then absent in many by the 5th day of life. The progress of these newborn infants has been followed and in none has evidence of dysplasia of the hip developed subsequently. Many of these infants represented breech presentations. We have not felt that the presence of Ortolani's sign alone in the newborn infant warrants roentgenographic examination, the diagnosis of dysplasia, or treatment.

We have found inequality of thigh creases both as to number and as to depth to be of little value in the early detection of congenital dysplasia of the hip with luxation. The same may be said for the gluteal creases and the length of the legs. Furthermore, these signs may not be present in an infant with bilateral dislocation, and certainly the observations of inequality of creases and of apparent discrepancy in the length of the legs should alert one to the possibility of dysplasia of the hip. However, in most instances, one need not take roentgenograms unless there is also a positive result with the abduction test.

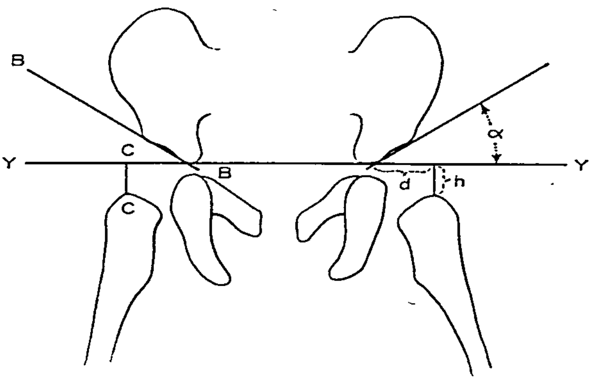

Fig. 2.—Drawing to illustrated Hilgenreiner's measurements. *Lines drawn:* YY, line drawn through Y cartilages to touch visible tips of ilia; *BB*, line drawn tangentially to visible acetabular face and through medial and lateral bony edges of acetabular face—difficult to draw accurately in newborn infant because of insufficient roentgenographic definition at this age; *CC*, line drawn from most cephalic point of femoral diaphysis and perpendicular to *YY* line. (Note: YY, *BB*, and *CC* lines designated as such by present authors for descriptive purposes.) *Hilgenreiner's measurements* α—angle between *BB* line and YY line, known as acetabular angle; *d*, distance between point of transection of YY line by *BB* line and point of transection of YY line by *CC* line, generally referred to as *d* line of Hilgenreiner; *h*, distance between most cephalic point of femoral diaphysis and point where *CC* line transects YY line. (Reproduced with permission from Harris, L. E., Lipscomb, P. R., and Hodgson, J. R.: Hilgenreiner Measurements of Hip Roentgenograms in 247 Normal Infants 6 and 7 Months of Age: Follow-up of Deviations From "Normal", J. Pediat. 56:478-484 [April] 1960.)

Roentgenographic Criteria

As previously noted, this report is concerned primarily with the use of the abduction test as a screening technique for detection of congenital disease of the hip. Detailed roentgenographic data will be given in a future report. However, the criteria we have used will be briefly noted.

Congenital Dysplasia of Hip with Luxation.—We have chosen to limit the diagnosis of congenital dysplasia of the hip to those infants who showed roentgenographic evidence of luxation. Hilgenreiner's[3] measurements have been used as described in figure 2. The characteristics of the group designated as having "congenital dysplasia of the hip" include the Putti[4] triad of upward displacement of the upper end of the femur, sloping acetabular roof (that is, increased acetabular index), and poorly developed epiphysial nucleus. In addition, all these infants except those in whom dysplasia was discovered in the newborn period have shown an iliac stress line (fig. 3). Figure 4 represents a typical example of this group. We have used the term "luxation" to mean displacement, complete or incomplete.

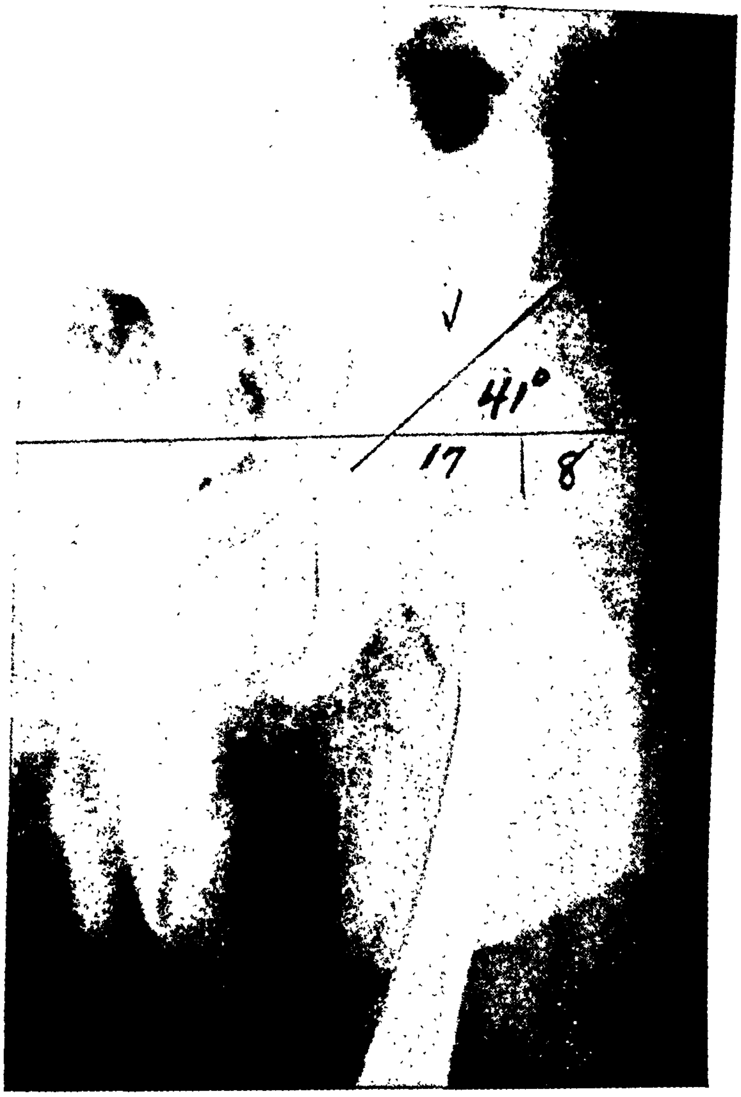

Fig. 3.—Iliac stress line in 4-month-old infant with congenital dysplasia and luxation (incomplete) of hip.

Probable Congenital Dysplasia of Hip.—The infants with probable congenital dysplasia of the hi were those who had a positive result with th abduction test, increased measurable acetabular angles, and subsequently also a delay in appearance of the ossification of the capital femoral epiphysis but did not show displacement of the head of the femur. Figure 5 represents an example of this category.

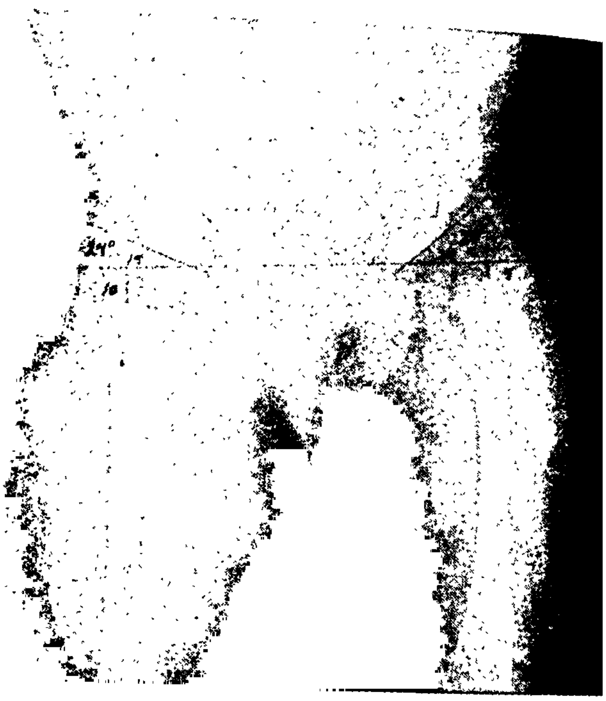

Fig. 4.—Congenital dysplasia of hip with luxation.

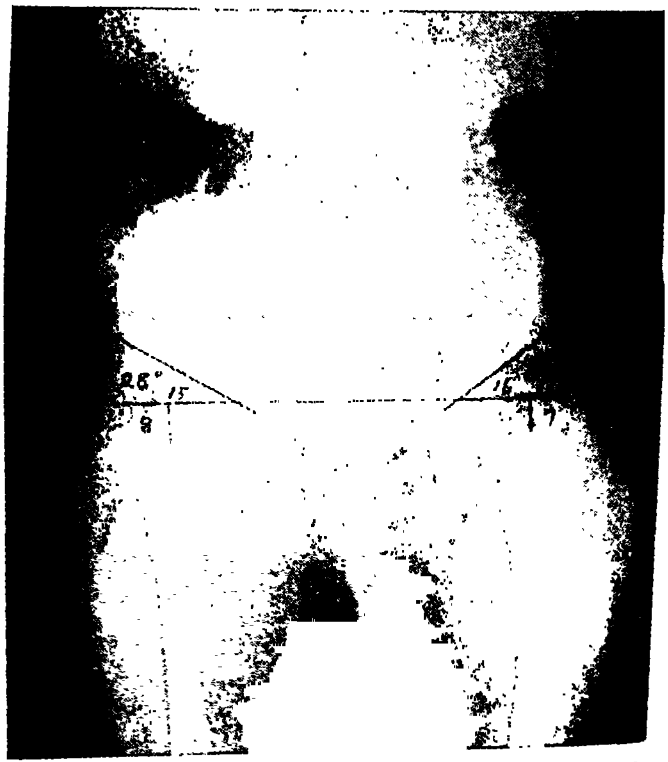

Fig. 5.—Probable congenital dysplasia of hip in 3-month-old infant. No definite luxation is evident although iliac stress line is.

Comment

The fact that older children with frank dislocations of the hip continue to be seen seems to emphasize the need for continuous and adequate physical examinations during the first year of life, if congenital dislocation of the hip is to be diagnosed early. It is well recognized that most infants do not have regular examinations during the first year; they receive their medical care through the overworked and harassed general practitioner who simply does not have the time available for regular monthly examinations of the infants under his care. Perhaps an effort to educate mothers in the application of the abduction test would be justifiable. It is a simple test to perform; indeed, in areas of Italy[5] where there is a high incidence of congenital disease of the hip the mothers have been indoctrinated in the signs that may indicate dislocation. At present, in addition to constant education of physicians in the methods of early diagnosis, public education would seem to offer a great opportunity for early recognition. Such methods would undoubtedly lead to a great deal of confusion for some time but they might be worth it.

We have not discussed methods or results of treatment. The problem of diagnosis is the responsibility of all physicians dealing with children, while the problem of treatment should be in the hands of the orthopedic surgeon. Although results of treatment will be presented in detail in a future report, it may be stated without hesitation that early diagnosis and treatment have greatly improved the final outcome of congenital dysplasia of the hip with luxation.

Does the abduction test always give a positive result in congenital dysplasia of the hip with luxation and in congenital dysplasia of the hip before luxation? In our experience, the result has always been positive when there is luxation, as shown by the fact that, apparently, the diagnosis has not been overlooked in about 9,000 infants, the youngest of whom is now more than 3⅓ years of age. Our experience also suggests that the abduction test may not give a positive result in many infants in the predislocation phase. We arrived at this opinion because all the infants having dysplasia and luxation were examined at monthly intervals and they did not have a definitely positive result of this test prior to the time of diagnosis (average age, 4 months). If one might assume that at least some of the infants in the category of those having "probable dysplasia" would have experienced luxation at a later age and that the abduction test always gave a positive result in the predislocation phase, then the group with eventual luxation should have been discovered at an earlier age than the average of 4 months. The abduction test may not be successful in diagnosing dislocation in the retarded and extremely hypotonic infant, the infant with severe spasticity, or the infant with myelodysplasia and flaccid paralysis of the legs. No doubt, some infants with dysplasia and dislocation do not demonstrate a positive result with the abduction test, but we have not seen such an infant who was otherwise normal.

Our study included those infants born from Jan. 1, 1949, through Dec. 31, 1955. At the time of this report (July, 1959), still no infants examined within 24 hours of birth and cared for by pediatricians in the well-child clinics have shown dislocation of the hip at the weight-bearing age. The average age at diagnosis of those with congenital dysplasia of the hip and luxation has remained essentially unchanged (4 months).

Summary and Conclusions

The search for a simple effective means for the early diagnosis of congenital disease of the hip continues. At present, the abduction test seems to be the most easily applied test to accomplish this end. It is simple to perform and requires a minimal degree of experience for adequate interpretation.

This report presents the results of use of this test as a screening procedure in 11,010 newborn infants, about 90% of whom were subsequently examined regularly in well-child clinics. With this test, the average age at diagnosis of congenital dysplasia with dislocation was reduced from 14 to 4 months, with no dislocations being undiscovered prior to the weight-bearing age.

A negative result of the abduction test at birth does not rule out potential dislocation of the hip. The test should be done regularly during the first 12 months of life.

While of limited value, other clinical signs suggestive of congenital dislocation of the hip should not be ignored. These signs may be of little value in infants with bilateral dislocation.

On the basis of roentgenographic findings the infants were classified as (1) those with congenital dysplasia of the hip with luxation and (2) those with probable congenital dysplasia.

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J.A.M.A., May 21, 1960

CARCINOMA OF THE GALLBLADDER—A REAL HAZARD

SUMMARY OF TWENTY CASES

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The authors reviewed 645 gallbladder operations performed by one of them during a 22-year period to determine whether cancer of the gallbladder occurs frequently enough in private practice to be considered a real threat to life. Of 320 patients who were 50 years of age or older having gallstones, there were 20 with carcinoma—an incidence of 6%. Because of delays, removal of the gallbladder was possible only in 8 of the 20 patients. For 18 of the 20 patients the average survival time was 151 days; the 2 surviving at the time of writing had metastases. Since 1 in 16 patients 50 years of age or older, having gallstones, will develop carcinoma, the authors consider carcinoma a real hazard in gallbladder disease and plead for earlier surgery.

A century ago carcinoma of the gallbladder was considered an extreme rarity, but today it ranks sixth among malignant neoplasms of the digestive tract[1] and causes an estimated 6,500 deaths annually in the United States.[2] The literature abounds with numerous reports based on autopsy findings or on collective clinical experience.[3] Few, however, reflect the findings of a single observer.

Subjects and Procedures

Our interest in the subject stems from our experience with two patients with gallstones who refused surgical intervention for 9 and 15 years, respectively, only to succumb finally to carcinoma of the gallbladder. We were further disturbed by the many authors who minimize the danger of malignancy of the gallbladder. Again, many of our patients with carcinoma of the gallbladder harbored stones for many years but were advised against surgical intervention by their physicians who believed that the mythical "silent gallstones" should not be disturbed.

We therefore undertook a review of all the operations on the gallbladder performed by one of us (A. H.) from July 1, 1937, to July 1, 1959, to determine whether cancer of the gallbladder occurred frequently enough in our private practice to consider it a real threat to life and thus a true indication for surgical intervention.

Incidence.—Of 645 patients who had cholecystectomies performed (stones being found in about 98%), 488 underwent elective operations, without any postoperative deaths. Of 137 patients with acute illness, 6 (4.6%) died postoperatively. Of 20 patients with carcinoma, 4, or 25%, died postoperatively. The gross incidence of 20 cancers occurring in 645 cases thus equals 3.1%. Since all the carcinomas occurred in patients 50 years of age or older (table 1), the more correct incidence is 20 of 324 persons (50 years or older), or 6.2%.

Symptoms.—As noted in table 2, the symptoms were usually those of any patient with gallbladder disease. Only two patients denied having symptoms, and these were discovered during an exploration incidental to an abdominal hysterectomy.

Although two-thirds of the patients had had recurrent episodes of right upper abdominal pain or epigastric distress, for as long as 30 years in some cases, the character of the pain in the patients with carcinoma had changed to a persistent, severe, unrelenting pain. It was the change in character of the pain which forced the patient, at long last, to seek relief.

The next most frequent symptoms which persuaded the patient to seek surgical advice were weight loss and jaundice. The condition of the jaundiced patient was usually misdiagnosed as common duct stone or malignancy of the head of the pancreas.

On physical examination, a hard mass was palpated in the right upper part of the abdomen in 45% of the patients. Several had enlarged livers and were obviously suffering from metastatic cancer. In those patients who were given roentgenographic examinations (10, or 50%), calculi were observed in 3 and were not visualized in 7. There was nothing in the roentgenographic examination, however, that pointed to the diagnosis of malignancy.

Operative Findings.—At operation, five patients had acutely inflamed gallbladders, one with a free perforation. One had hydrops. In most patients there was direct extension of the carcinoma either to the liver or to adjacent organs, such as the stomach, duodenum, pancreas, or omentum. Only

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eight of these carcinomas were in a sufficiently early stage to allow performance of a cholecystectomy. Twelve other patients underwent such procedures as cholecystostomy and biopsy.

Gallstones were absent in only one case. Of the remaining 19 patients, 18 had stones and 1 had a very firm, stony-hard gallbladder which was not opened. This patient had a nonfunctioning gallbladder at roentgenographic examination and was presumed to have stones. All lesions were adenocarcinomas; two were papillary tumors, and one showed squamous metaplasia.

Table 1.—*Age and Sex of Patients with Carcinoma of Gallbladder*

	Sex		
Age, Yr.	Male	Female	Total
50-59	1	7	8
60-69	1	6	7
70-79	1	3	4
80-89	..	1	1
Total	3	17	20

Postoperative Course and Follow-up.—There were four deaths in the immediate postoperative period, on the 2nd, 3rd, 11th, and 16th day respectively. All except 2 of the patients are dead at the time of writing. The two living patients have metastases. The survival period ranged from 1 month to 20 months, the average being 151 days. One of the survivors is only a few months beyond the operation. The other has survived nine years postoperatively, and her case is of sufficient interest to warrant a more detailed discussion.

Report of Cases

Case 1.—A 63-year-old woman had a 30-year history suggestive of gallbladder disease. The gallbladder was not visualized on roentgenographic examination. Physical examination was noncontributory. On Aug. 30, 1950, a routine cholecystectomy was performed. Pathological examination confirmed the presence of stones, but, in addition, revealed a small, localized papillary adenocarcinoma in the fundus.

The patient did well until April, 1958, when she developed jaundice and on reexploration elsewhere, a papillary adenocarcinoma of the right hepatic duct was found and removed. In November, 1958, she had a recurrence of jaundice, and on reexploration a recurrence of the tumor, with metastases, was found. At the time of writing she is still alive, with a T-tube in place.

Comment.—The 6% incidence of carcinoma of the gallbladder in patients aged 50 years or older with gallbladder disease should be sufficient reason to jolt physicians who are complacent about gallstones. No longer may these physicians in good conscience shrug off gallbladders with gallstones with the casual remark, "If they don't bother you, don't bother them." Perhaps the following report is a case in point.

Case 2.—A 57-year-old woman was found to have a gallbladder full of stones at routine exploration during performance of an abdominal hysterectomy for fibroids. After her recovery from the operation, she was advised to have a cholecystectomy. She demurred, denying that she had ever suffered from "indigestion" of any kind. After being advised against delay, she finally decided three weeks later to have a cholecystectomy.

At operation we were astounded to find that, in addition to multiple stones, there was a carcinoma in the fundus of the gallbladder. A small, pea-sized nodule in the liver, which was thought to be inconsequential at the time of its removal, proved to be a highly anaplastic metastatic lesion. She died seven months postoperatively.

Comment.—The disease was so far advanced when first seen that in only 8 of the 20 patients with carcinoma of the gallbladder was it possible to perform a cholecystectomy. It also accounts for the 25% operative mortality.

When carcinoma of the gallbladder occurs in 1 of 16 patients aged 50 years or older who suffer from a diseased gallbladder, it can no longer be termed a rare disease. Perhaps there are a number of carcinomas of the gallbladder which escape detection. This happened in one of our cases, in a jaundiced patient who at operation was thought to have carcinoma of the head of the pancreas. At autopsy, however, the primary carcinoma was found to have begun in the gallbladder. Hence, since life expectancy, once the diagnosis of carcinoma is made, can be counted in months, we must conclude that it most certainly constitutes a real threat to life.

Table 2.—*Symptoms of Patients with Carcinoma of Gallbladder*

	Patients	
	No.	%
Pain	17	85
Indigestion	8	40
Jaundice	6	30
Weight loss	6	30
Anorexia	5	25
Nausea and vomiting	3	15
None	2	10

In a previous communication[4] it was pointed out that there is a greater incidence of acute cholecystitis, common duct disease, gangrene, and perforation, as well as malignancy, in the aging patient with gallstone disease. As noted before, there was no mortality in patients who had elective operations but a 4.6% mortality in those with acute cases. This latter mortality can also be avoided by the early removal of the calculous gallbladder.

Summary and Conclusions

In our opinion, based on 20 cases of carcinoma of the gallbladder in our practice, one patient in 16, aged 50 years or older and usually a woman, with gallstones will probably develop carcinoma of the gallbladder. She usually will have the ordinary symptoms of gallbladder disease. If the character of the pain becomes persistent, however, there is great danger that a malignant change may have developed. If, in addition, there is concomitant weight loss and a hard palpable mass in the right upper part of the abdomen, the diagnosis of carcinoma is almost certain. Once the diagnosis of carcinoma of the gallbladder is confirmed, the life expectancy is but a few months.

We can only conclude that if this gloomy outlook is to be brightened, a more aggressive attitude must be taken toward the eradication of gallstone disease. The only "silent" gallstone is the one in a bottle. We must repeat our previous statement,[4] ". . . gallbladders with gallstones should be removed before they become vocal. For if they begin to shriek with malignant changes, it is often too late."

Addendum

Since acceptance of this contribution for publication, the remaining two patients who survived operation have died.

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SURGICAL TREATMENT OF POSTINFARCTION VENTRICULAR ANEURYSMS

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The disability caused by ventricular aneurysms and the possibility of repairing them by surgical excision are illustrated in these case histories of three patients. Two were men, aged 44 and 56 years, and one was a woman aged 55 years. The operations consisted of open cardiotomy with temporary heart-lung bypass, removal of the aneurysm, and suturing of the ventricle. The resulting improvement of cardiac function was shown by clinical tests and physiological measurements, and all three patients have returned to their regular occupations.

The development of a ventricular aneurysm is a serious and fairly common sequel of myocardial infarction. Schlichter and co-workers[1] found ventricular aneurysms at autopsy in 20% of patients with myocardial infarction. The seriousness of the lesion is indicated by the death of 73% of these patients within three years and of 88% within five years of their infarction. In contrast, Master and co-workers[2] found that 50% of all patients having myocardial infarctions lived five years and 40% had a complete functional recovery. The major cause of death of the patients with ventricular aneurysm was congestive heart failure. About one-half the patients had an additional infarct, usually in the area of the aneurysm. One-half had arterial embolic phenomena, and in one-third the emboli were a main or contributing cause of death.

The pathological features of the aneurysm help to explain its physiological effects. Usually there is a thin wall of fibrous tissue, tough but noncontrac-

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tile and clearly demarcated from the adjacent trabeculated myocardium. It is lined by thrombus, firm and well organized at the periphery but soft and friable near the ventricular lumen. Its paradoxical motion at each systole greatly reduces the effective stroke volume, thus placing an increased burden on the remaining functional myocardium. Rupture of a ventricular aneurysm is infrequent, perhaps because its tough fibrous wall is usually supported by adherent pericardium.

The most important diagnostic finding is the presence of a bulge with paradoxical pulsations, usually on the anterolateral wall or apex of the left ventricle. The electrocardiogram shows evidence of an old infarct. A history of myocardial infarction, particularly in a hypertensive patient or one treated by early ambulation, is helpful.

In spite of the occasional long-term survival of a patient with a ventricular aneurysm,[3] the proper treatment is surgical excision, which restores the integrity of the ventricular wall and removes the source of arterial emboli. In 1931 Sauerbruch[4] excised an aneurysm of the right ventricle thought to be due to myocarditis. This patient was well three and one-half months later. In 1942 Beck[5] performed a plication for a ventricular aneurysm on a 49-year-old man and reinforced it with fascia lata. Infection caused the patient's death five weeks later. In 1947 Murray[6] reported the results of excision of acute myocardial infarcts in dogs. He demonstrated the paradoxical motion of the infarcted area and the improvement in the animal's circulatory status that followed its removal. Bailey and co-workers[7] reported the subtotal resection of postinfarction aneurysm in six patients, five of whom survived and achieved clinical improvement. A special clamp was used to permit the subtotal resection of the aneurysm from the functioning heart. DeCamp[8] also used a clamp to excise a left ventricular aneurysm, but the patient died on the eighth day of a fresh infarct. Cooley and coworkers[9] described the removal of postinfarction ventricular aneurysms in two patients, with use of temporary heart-lung bypass. Both patients survived. Cardiac catheterization studies in the second showed return to normal of pulmonary artery pressure and cardiac output after operation. Cooley and co-workers[10] later reported operations on ten patients with ventricular aneurysms. Eight survived and attained clinical improvement. Physiological studies confirmed this improvement.

Method.—We have operated on three patients with postinfarction ventricular aneurysms, using temporary heart-lung bypass with the Gibbon heart-lung machine. All three patients survived and are in much improved condition, two 18 and one 11 months after operation. A bilateral, sternum-dividing, anterior thoracotomy was performed. After the conventional cannulations, heart-lung bypass was established. The pericardium was separated from the aneurysm to permit identification of the coronary arteries, which in all cases ran close to the margins of the aneurysm. The aneurysm was then widely incised and the thrombus removed (fig. 1, *left*). The intracardiac structures, particularly the large anterior papillary muscle (fig. 1, *center*) were visualized, and the aneurysm was excised at its easily identifiable junction with thick, viable, trabeculated muscle. The ventriculotomy was then closed by approximating muscle to muscle with a row of interrupted mattress sutures oversewn with a continuous suture (fig. 1, *right*).

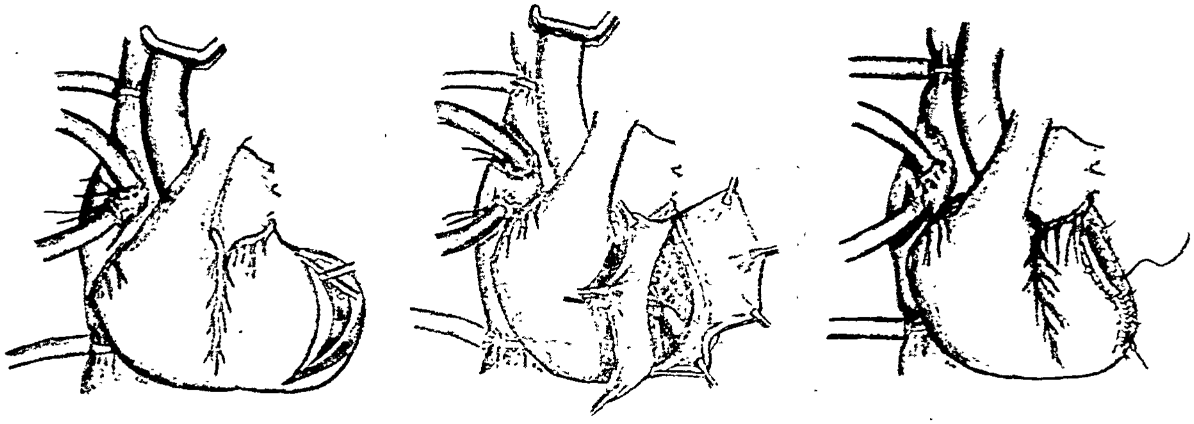

Fig. 1.—Techniques of excising aneurysm. *Left*, wide incision of aneurysm and removal of thrombus. *Center*, intracardiac structures, particularly large anterior papillary muscle, visualized and aneurysm excised at identifiable junctions with trabeculated muscle. *Right*, closure of ventriculotomy by approximating muscle to muscle with row of interrupted mattress sutures oversewn with continuous suture.

Report of Cases

Case 1.—A man aged 44 years was admitted to the Jefferson Medical College Hospital in January, 1958. He had been well until Sept. 26, 1957, when he sustained a myocardial infarction while at work as a pipe fitter. He was admitted directly to another hospital where he stayed at rest in bed for one month. This was followed by three weeks of bed rest at home and gradual increase in his activity. Increasing dyspnea developed so that by January, 1958, three months later, he could no longer lie down and spent his nights sitting in a chair. He was readmitted to the hospital where a diagnosis of ventricular aneurysm was made and he was transferred to Jefferson Medical College Hospital.

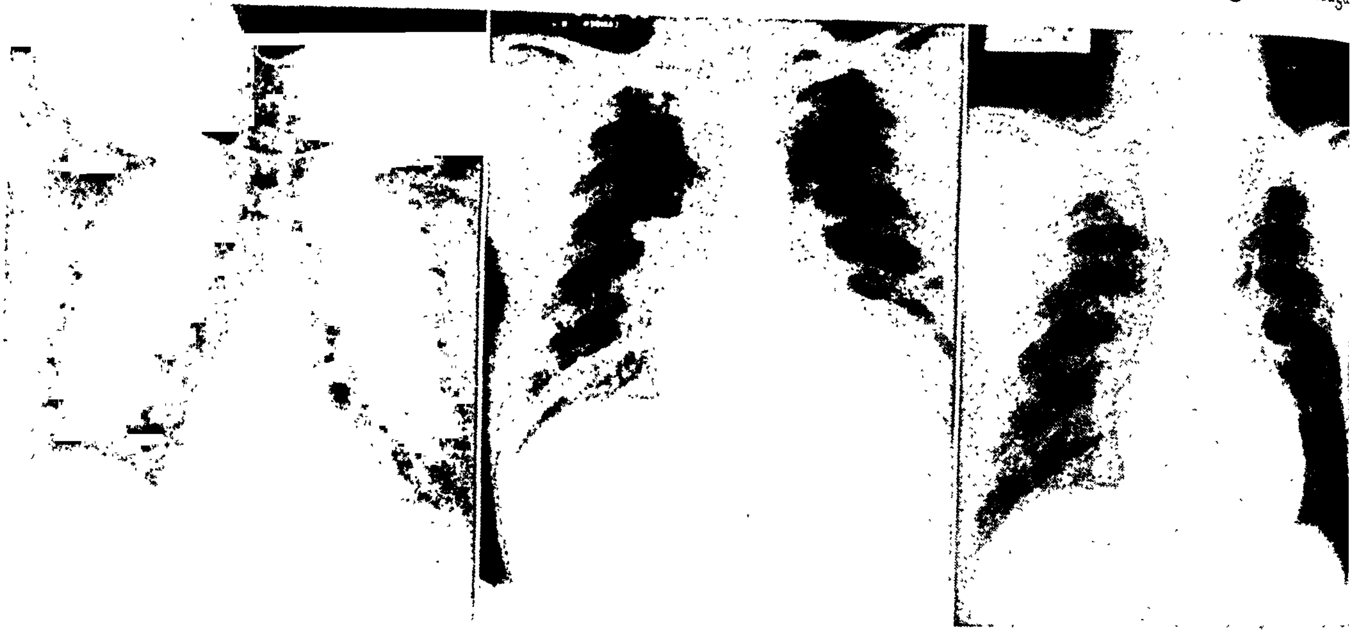

Fig. 2 (case 1).—Chest roentgenograms. *Left*, day of infarction. *Center*, 16 weeks after infarction. *Right*, 17 months af operation.

The left ventricular aneurysm was removed on Feb. 13, 1958. Since that time his condition has shown marked and continued improvement. Two months after operation he began regular work as an office worker. At the time of writing, 18 months after operation, he has no symptoms referable to his circulatory system. He is never unduly tired, can walk as far as he wishes, and participates in normal activities. Results of physical examination have been normal. Figure 2, *left*, shows the chest roentgenogram on the day of infarction, and fig. 2, *center*, 16 weeks later. The appearance 17 mo after operation is shown in figure 2, *right*.

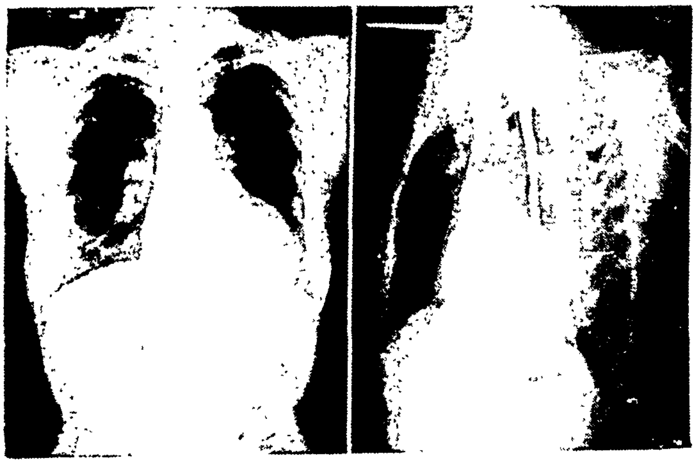

Fig. 3 (case 2).—Chest roentgenograms. *Left*, before operation. *Right*, 17 months after operation.

Case 2.—A 55-year-old woman was admit to the Jefferson Medical College Hospital in Fe ruary of 1958. She had no clear-cut history of my cardial infarction. In 1953 and again in Aug 1957, however, she had attacks of severe pain her left arm and shoulder. On both occasions had stayed away from work for two days, but diagnosis of infarction was not made and no th apy was given. After the second attack she dev oped a severe cough and dyspnea which we progressive, leading to her hospitalization in Jan ary, 1958. A diagnosis of left ventricular aneury was made five months after the last attack of p She was transferred to Jefferson Medical Col Hospital, and the aneurysm was removed on Fe 25, 1958. At the time of writing, 18 months aft operation, she is working regularly as a secreta She has no symptoms and carries out normal act

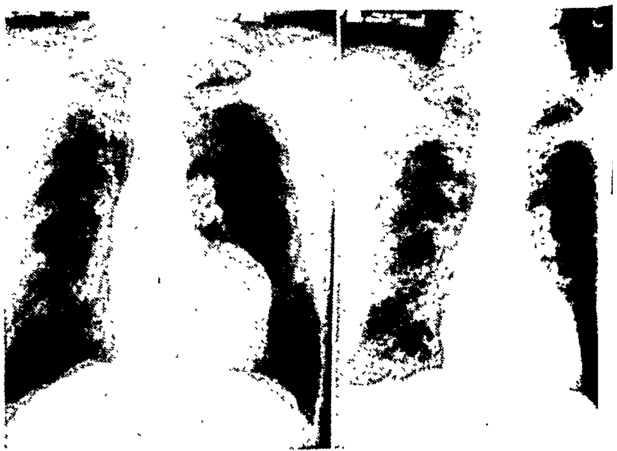

Fig. 4 (case 3).—Chest roentgenograms. *Left*, bef operation. *Right*, after operation.

ities. Findings of physical examination have been normal, except for a grade 1 systolic murmur at the apex which is not transmitted. The rather unusual posterior position of this aneurysm is shown in figure 3, *left*, and the appearance 17 months after operation in figure 3, *right*.

Case 3.—A 56-year-old man was admitted to Jefferson Medical College Hospital in September, 1958. His first myocardial infarction had occurred on May 16, 1957. He was kept at bed rest for one month, after which he gradually increased his activities and returned to work in September, 1957. During the ensuing months he had occasional attacks of anginal pain, relieved by nitroglycerin. A second infarction occurred on May 1, 1958. Again he was kept at bed rest for one month, after which he gradually increased his activities. He had no more anginal pain but increasing dyspnea, a chronic cough, and a pulsation in the left side of his chest that prevented return to work. A large anterolateral left ventricular aneurysm was removed on Sept. 25, 1958. His condition was markedly improved 11 months after operation. He has no symptoms referable to the circulatory system and has been working regularly since March, 1959. Findings of physical examination have been normal. Figure 4, *left*, shows the chest roentgenogram before and figure 4, *right*, after operation.

All three of these patients had cardiac function studies performed after operation and two of them before. Cardiac outputs were determined by the dye injection technique.[11] Blood oxygen saturation determinations and oxygen consumption studies were done. The results of these studies are shown in the table. The first patient, who was completely incapacitated before operation, had normal cardiac function nine months afterwards. The second patient showed marked improvement in cardiac output, stroke volume, and arteriovenous oxygen difference nine months after operation. The third patient's condition showed similar improvement. Of particular interest in this patient is the change in his stroke volume with exercise. In the presence of the aneurysm, the stroke volume diminished with exercise, but after the aneurysm was removed exercise was accompanied by an increase in stroke volume.

Results of Cardiac Function Studies in Three Patients Subjected to Surgical Removal of Postinfarction Ventricular Aneurysms

	Patient 1		Patient 2		Patient 3			
	9 Mo. After Operation		Before Operation	9 Mo. After Operation	Before Operation		1 Mo. After Operation	
	Rest	Exercise	Rest	Rest	Rest	Exercise	Rest	Exercise
Cardiac output (liter/min.)	4.9	5.7	3.1	6.4	5.2	5.74	6.6	8.7
Cardiac index	2.9	3.3	2.1	4.3	2.8	3.08	3.6	4.8
Stroke volume (ml.)	68	69	41	73	63	57	80	94
Arteriovenous O_2 difference (vol. %)	5	6	6	3	7	8	3.3	5.0
O_2 consumption (ml./min.)	293	366	179	192	366	478	224	455
O_2 consumption (ml./min./sq.m.)	168	210	120	129	200	266	125	253

Comment

These three patients, incapacitated before operation, have shown marked improvement after removal of their ventricular aneurysms, as shown by their clinical states and the physiological studies. All three tolerated the operation well and are working regularly and carrying out normal activities, two 18 and one 11 months later respectively. The ability of these patients to (1) survive an infarction severe and extensive enough to produce the aneurysm and (2) survive the presence of the aneurysm itself helps to explain their excellent response to operation. In the excision of these lesions, open cardiotomy with temporary heart-lung bypass has definite advantages over the closed method. The occurrence of arterial emboli can be avoided, and the surgeon can be sure of removal of all thrombus from within the ventricular chamber, which, if necessary, can be emptied of its blood and irrigated with saline solution. The aneurysm can be completely excised up to viable myocardium, which can be accurately sutured. Damage to intracardiac structures and to coronary vessels can be easily avoided.

Summary

Postinfarction ventricular aneurysms cause death and disability from circulatory failure or arterial emboli. Ventricular aneurysms are surgical lesions and should be excised. Excision is followed by marked improvement in circulatory status. Temporary heart-lung bypass permits safe removal of the aneurysm and satisfactory repair of the ventricle.

Addendum

An additional patient, 16 years of age, with an acquired left ventricular aneurysm was operated on Dec. 17, 1959. He was well four months later. The other patients continued a satisfactory course, two 26 and one 19 months after operation.

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PERNICIOUS ANEMIA MASKED BY MULTIVITAMINS CONTAINING FOLIC ACID

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The danger of administering folic acid preparations without specific indications is illustrated by two case histories. Two women, aged 58 and 70 years, complained of paresthesias, difficulty in walking, and other neurological symptoms. The diagnosis of pernicious anemia as the underlying disease was not clear until it was discovered that the first patient had been taking folic acid preparations daily for more than two years; the other had been doing so for more than a month. After the correct diagnosis had been made, use of the folic acid was discontinued, and treatment with liver extract and vitamin B_{12} was followed by some relief of the neurological symptoms. A plea is made for the elimination of folic acid from multivitamin and iron preparations.

The clinical features of pernicious anemia were fully described by Addison in 1855. Biermer,[1] apparently without the knowledge of Addison's previous account, wrote a more comprehensive description in 1872.

The diagnosis of pernicious anemia is frequently missed today, despite modern diagnostic aids and voluminous literature on this subject. Confusion in the diagnosis of pernicious anemia is brought about by the indiscriminate administration of liver extract and vitamin B_{12} by physicians for various complaints. To further confuse the issue, Pfieffner and co-workers[2] crystallized vitamin B_c in 1943. Angier and others, in 1946, identified vitamin B_c as a conjugate of pteroylglutamic acid and synthesized the compound. After this, folic acid was included in multivitamin preparations by many pharmaceutical companies, without adequate therapeutic evidence of need.

Shortly after the introduction of folic acid for the treatment of anemia, Moore reported a therapeutic failure, in a patient with spinal cord degeneration, at the 1946 meeting of the Society for Clinical Investigation. This report was followed by others from Bethell and co-workers,[3] Hall, Watkins, and Hargraves,[4] Vilter, Vilter, and Spies,[5] Ross, Belding, and Paegel,[6] Heinle and Welch,[7] and Schwartz, Kaplan, and Armstrong.[8]

Many other studies revealed that folic acid could induce a hematological remission in pernicious anemia but did not prevent neurological symptoms from appearing, nor did massive doses of folic acid halt or reverse the degenerative process once it had begun.

After these and other reports appeared in the literature, an editorial in the *New England Journal of Medicine*[9] warned against the use of folic acid. This editorial pointed out that there were three possible relations of folic acid to neurological dis-

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turbances: first, folic acid may merely be allowing the disease to run its natural course; second, Heinle and Welch suggested that folic acid, in relieving one deficiency, accentuated another; and third, folic acid may actually exert positively deleterious influences on the nervous system.

In 1953, Wintrobe[10] emphatically stated, "Folic acid can produce an hematopoietic response in pernicious anemia but does not protect the nervous system. Consequently, its use in the treatment of that disease is dangerous. Only in the very rare disorders, 'Achrestic anemia' and 'refractory megaloblastic anemia' and in the uncommon conditions, megaloblastic anemia of infancy, and 'pernicious anemia of pregnancy,' as well as in some cases of sprue, idiopathic steatorrhea and nutritional macrocytic anemia, does folic acid have a place in the treatment of anemia."

Conley and Krevans,[11] during 1950, recognized and diagnosed pernicious anemia in five patients with essentially normal blood findings and neurological findings compatible with degeneration of the spinal cord. These five patients had been taking multivitamin capsules. The preparation taken was identified in four patients and found to contain from 0.75 to 5.0 mg. of folic acid per capsule. One patient had taken a capsule containing 5 mg. of folic acid intermittently for two years, whenever he felt tired. The second patient had taken a total of 8 mg. of folic acid daily for two and one-half years. The third patient had taken six vitamin capsules daily (0.75 mg. of folic acid each) for over three years. The fourth patient had taken three capsules daily (1.7 mg. of folic acid each) for five months. The fifth patient had taken multivitamin capsules of undetermined potency for one year. All five of these patients responded satisfactorily to parenteral therapy with vitamin B_{12}.

In 1952, DeWit[12] reported the case of a patient who had taken 3 mg. of folic acid daily in multivitamin capsules and developed neurological symptoms. When the patient was first seen, the blood findings were essentially normal. The neurological symptoms responded to parenteral therapy with vitamin B_{12}. The patient stopped having the injections and later developed a pathological blood picture and neurological changes compatible with pernicious anemia. Reinstitution of parenteral therapy with vitamin B_{12} was again effective in reversing the neurological changes and producing a normal blood picture.

Report of Cases

Case 1.—A 58-year-old woman was first seen on May 15, 1950, and supervised until Jan. 20, 1955. On admission she complained of numbness and tingling of the fingers to the wrists, of two years' duration, and numbness and tingling of the feet and lower legs, of two months' duration; marked weakness and fatigue were present, along with "stumbling when she walked." The "soles of the feet felt thick." She had many symptoms of an anxiety tension state and was emotionally disturbed over domestic difficulties.

The contributory physical findings on examination were a markedly decreased left-sided patellar reflex, normal on the right side. Both achilles tendon reflexes were absent with reinforcement, arm reflexes were normal, vibratory sensation, to a C 256 tuning fork, was present in the arms but absent from both iliac crests to the feet. Romberg's sign was not present, and there was decreased touch sensation of the feet and normal response to pain stimulus. Proprioceptive sensation in the toes was considered decreased. The arterial pulsations were normal.

Laboratory reports were as follows: result of urinalysis normal, fasting blood sugar level 110 mg.%, blood cholesterol level 289 mg.%, sedimentation rate 12 mm. in one hour (Westergren), and basal metabolic rate —18. Spinal fluid examination showed normal pressure, no blood cells, total protein content 55 mg.% (normal 25-45), a trace of globulin, and negative result of the Kolmer-Wassermann test. A roentgenogram of the cervical spine showed marked hypertrophic changes in the lower portion. The complete blood count showed the hemoglobin concentration to be 13.0 Gm.%, red blood cell count, 3,900,000 per cubic millimeter, color index 1.09, and 7,600 white blood cells per cubic millimeter, with 46% lymphocytes and 54% segmented cells. The blood smears showed slight anisocytosis. There were no macrocytes or megalocytic or nucleated red blood cells, and the granulocytes appeared normal. A gastric analysis, made with use of 100 cc. of 7% alcohol, followed by histamine, showed no free hydrochloric acid.

After extensive questioning about anemia and previous medication, the patient stated she had been taking two or three "vitamin capsules" daily since January, 1948. These capsules contained concentrated extract of stomach, 0.324 Gm.; ferrous sulfate, 0.130 Gm.; vitamin B_1 mononitrate, 0.5 mg.; vitamin B_2, 0.25 mg.; and folic acid, 1 mg. It was also determined that she had been taking another preparation twice daily since May, 1948, which contained dried ferrous sulfate, 0.194 Gm., and folic acid, 1.7 mg., in each capsule.

After these findings were considered, a diagnosis of pernicious anemia with degeneration of the spinal cord was made, and 30 units of concentrated liver extract was given daily. The maximum reticulocyte response was obtained six days after liver injections were started, at 1.7%. In three months, the hemoglobin level stabilized at around 13.0 Gm.%, with 4,300,000 red blood cells per cubic millimeter.

On this therapeutic program, vibratory sensation returned to the patient's ankles in three months and the dose of liver extract was reduced to 30 units three times weekly; in seven months dosage was reduced to once weekly. Four and one-half years from the date the patient started to take liver extract she still complained at times of paresthesias of the feet and hands. Vitamin B_{12} was substituted for concentrated liver extract in 1953, 100 mcg. per cubic centimeter every 10 days, and later 1,000 mcg. at weekly intervals was given in an attempt to eradicate the paresthesias, without complete success.

Case 2.—A 70-year-old woman was admitted to Charleston Memorial Hospital on March 16, 1956, and discharged April 10, 1956. Her complaints on admission were numbness of the fingers of both hands of two months' duration and paresthesia of the legs and difficulty in walking of one month's duration; she denied any pain or soreness of the tongue.

The contributory physical findings on examination included blood pressure 150/80 mm. Hg, temperature 99 F (37.2 C), and gray hair with a fine texture. Neurological examination showed the cranial nerves to be intact, but astereognosis was present. Results of finger-to-nose and heel-to-knee tests were normal and position sense of the toes was questionable. The result of a Romberg test was positive and vibratory sensation, to a C 256 tuning fork, was absent in the ankles and knees and decreased in wrists.

The laboratory data included normal results of urinalysis, normal levels of nonprotein nitrogen, blood sugar, blood cholesterol, and total proteins, and normal albumin to globulin ratio. Sedimentation rates of 32 and 35 mm. in one hour (Westergren) were obtained. Spinal fluid examination was normal. Three stool specimens were negative for occult blood. Basal metabolic rate was —7 and result of serologic test for syphilis negative. Gastric analysis with histamine showed no free hydrochloric acid.

Multiple complete blood counts were obtained, showing hemoglobin levels of from 13.8 to 14.0 Gm.%, with, initially, 5,200,000 red blood cells per cubic millimeter, hematocrit reading 47%, white blood cell count 6,050 per cubic millimeter, and differential blood smear showing 48% lymphocytes, 48% segmented cells, and 4% eosinophils. Platelets numbered 154,000 and 0.9% reticulocytes were seen. Marrow aspiration and peripheral blood smears showed no abnormalities.

Roentgenograms of the entire spine showed moderate osteoporosis and marked hypertrophic changes in the lower cervical and upper thoracic area. The patient's history revealed that she had been anemic, "blood down to 40" during 1953, that some physician had given her "vitamin B_{12}" by mouth fo three or four months, and that then the bloo count was said to be normal.

On Dec. 9, 1955, the patient was admitted t another hospital for a diagnostic dilation an curettage because of postmenopausal bleeding tissue obtained was benign. That routine bloo count showed a hemoglobin level of 10.0 Gm. with a red blood cell count of 3,500,000 per cubi millimeter, a white blood cell count of 6,800 pe cubic millimeter, and a differential smear showin 59% segmented cells, 3% eosinophils, and 3 lymphocytes.

On Jan. 10, 1956, the patient entered Charlesto Memorial Hospital and had a vaginal hysterectom and pelvic repair. The complete blood count r vealed a hemoglobin level of 11.8 Gm.%; 3,900,0 red blood cells per cubic millimeter; and a whi blood cell count of 7,900 per cubic millimeter, with normal distribution of cells in the peripheral smea After operation, she had considerable difficulty wit urinary retention, which eventually ceased.

Further questioning revealed that the patie had been given a "shotgun" vitamin preparatio containing 22 ingredients. Our principal intere was in the folic acid content, 0.33 mg. per capsul of which the patient had taken at least three dai for one month and one or more daily since Dec. 1 1955. She stated, "If one was good, two or thr should be better."

On March 21, 1956, the patient started to r ceive daily parenteral injections of vitamin B (100 mcg.). The numbness of the extremities ha begun to disappear at the end of 11 days aft treatment was started. Vitamin B_{12} (1,000 mc and liver extract (20 units) was given by her hon physician twice weekly for two years and thr months. At the end of one year, the patient st required help in walking and had absent vibrato sensation in the ankles and absent patellar a achilles tendon reflexes. As of August, 1959, s could walk without assistance but continued have mild paresthesias of the feet and hands, a cording to her home physician.

Her blood count has been stationary at a hem globin level of about 12.0 Gm.%, with 4,000,0 red blood cells per cubic millimeter, for over tw years.

Comment

In the literature I have read of six cases o pernicious anemia in which signs and symptom have been altered by the ingestion of multivitamin capsules containing folic acid. Two more cases are presented here. There are, no doubt, many that have gone unrecognized or unreported.

The daily requirement of folic acid for the human being has not been determined.[13] On the basis of the requirements of other animals, the figure of 0.1 to 0.2 mg. per day has been suggested.[2] The average daily dietary intake is probably less than 10 mcg., according to Goodman and Gilman.[2] These authors also stated that only a small fraction appears in the urine from an orally ingested dose of 0.1 mg., but up to 90% is excreted when 15 mg. is ingested. It would appear that 1.0 mg. or less of folic acid daily might produce a hematological remission or precipitate a relapse, as seen in case 2.

Ross, Belding, and Paegel[6] maintained three of five patients in hematological remission on 1.25 mg. of folic acid daily. Reisner and Weiner[14] felt they obtained an adequate hematological response to 1.0 mg. of folic acid given orally and 0.25 mcg. of vitamin B_{12} given parenterally but not to orally given vitamin B_{12} (10 mcg.).

Heinle and Welch[7] speculated that folic acid not only failed to prevent neurological lesions but might precipitate their appearance. Further evidence that this might be possible was seen in a report by Lear and Castle.[15] These authors demonstrated that folic acid lowered the serum vitamin B_{12} level in 18 of 27 patients receiving vitamin B_{12} injections. If this is true, then it is conceivable that a patient who is in so-called remission might, by the added administration of folic acid, be thrown into hematological and neurological decompensation. This might have occurred in case 2 in this report.

The causes of hematological and neurological remissions in pernicious anemia are unknown. A remission may last from a few weeks to 15 years.[16] The length of time before relapse occurs in a patient with pernicious anemia depends on several variables[5]: (1) the amount of stored erythrocyte maturation factor; (2) the amount of intrinsic factor, however minute, produced by the stomach; (3) the amount of extrinsic factor(s) in the diet; and (4) the occurrence of infectious and degenerative diseases. To this list one might add (5) trauma, such as crushing injuries, surgery, and fractures, and (6) addition of folic acid to the diet or medication, in a patient with a borderline case of compensated pernicious anemia. Conceivably, the stress of surgery in case 2 could have hastened relapse. There are, perhaps, other causes of relapse in patients with pernicious anemia that are unknown at this time.

Summary

Two patients with pernicious anemia had the diagnosis obscured by the ingestion of vitamin preparations that contained folic acid. These patients developed degeneration of the spinal cord, not all of which was reversible with vitamin B_{12} therapy. It is my opinion, as well as that of many astute physicians, that folic acid should be removed from all multivitamin and iron preparations. Folic acid should be dispensed in individual tablets and used for those few specific conditions in which it is indicated.

It is anticipated that this report will call attention to this problem and stimulate further reports in the literature.

501 Atlas Bldg. (1).

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PATENT DUCTUS ARTERIOSUS AND THE OCCASIONAL CARDIAC SURGEON

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To investigate the results of patent ductus arteriosus surgery in the nonteaching areas, 448 inquiries were sent to hospitals in the large cities of the United States exclusive of those having medical schools and clinics of international renown. Information from 232 hospitals was reported on 508 operations. Of 320 patients whose patent ductus was obliterated by ligation, 12 died (3.6%). Of 188 who had the vessel closed by surgical division, 18 died (9.6%). These death rates were higher than those occurring in teaching medical centers. The reasons for this discrepancy are not necessarily with the surgeon alone but have a broader basis. The organization of a well-rounded cardiac surgical program including the diagnostic and operative teams is a responsibility of the total medical community.

It is generally agreed, by all who have studied the problem, that patent ductus arteriosus should be corrected surgically at an early age. The potential hazards and the reduced life expectancy in patients with uncorrected lesions are well recognized and documented in the surgical literature.[1] It is not the intention of this communication to challenge these views in any way.

Every conscientious surgeon is seriously concerned when he encounters mortality in a supposedly low-risk operative procedure. My investigations in this subject were prompted by the knowledge of several tragic results in patent ductus arteriosus surgery in local hospitals within the past few years. These consisted of three deaths at the hands of three different qualified surgeons, and two patients who were operated on by two other qualified surgeons for patent ductus arteriosus and whose diagnosis was found to be in error. While the latter two patients survived, facilities had not been arranged to correct the actual lesion encountered, and they were faced with the hazard of a second major operative procedure later. These five unfortunate local occurrences, within a total of 40 operations for patent ductus arteriosus, are cited as an introduction to some of the problems confronting the chest surgeon who attempts to perform cardiac surgery in a nonteaching area. Several major points of difficulty should be recognized.

First, while facilities for carrying out cardiac catheterization and angiocardiography may be available, these are often understaffed and manned by personnel whose time is overallotted to other duties. The resulting inertia can easily lead one into the fatal error of operating on a patient with "not quite typical" patent ductus arteriosus, without complete diagnostic procedures having been carried out preoperatively.

Second, surgeons who will undertake the correction of an occasional patent ductus arteriosus far outnumber the trained cardiac diagnosticians who have adequate financial support to run a modern diagnostic program in congenital heart disease. The causes of this major disproportion are manifold and not germane to this report. The result, however, is important in that the limited number of cases, adequately studied for surgery, are distributed among a number of surgeons. It is difficult for any one practicing surgeon to command enough continuous experience to maintain his proficiency. The work often averages about one case per surgeon per year.

Third, inadequate numbers of qualified anesthesiologists are present in most areas. The demands on their time in private practice are so great that it is sometimes difficult, or impossible, to secure their services. This occasionally results in this surgery being undertaken with the services of nurse anesthetists who may not be fully aware of all of the physiological problems related to blood volume and other features of patent ductus arteriosus.

Fourth, several factors compound the difficulty of establishing fixed surgical teams for cardiac surgery. These include the competitive and economic features of private practice and the infrequency of these cases.

Fifth, the house staff allotments can seldom be fulfilled, since the young medical graduate has a strong affinity for the teaching institutions. This results in a taxing work load for all hospital personnel. There are usually no resident physicians in thoracic surgery, and the general surgery resident has many other services to cover. The postoperative care is likely to fall almost entirely on the operating surgeon who may be busily engaged in surgery at another hospital across town when trouble arises.

Sixth, with the limited cardiac surgery available, the nurses are often unfamiliar with the standard principles of postoperative care, not to mention the early signs of complications. A continuous educational program is mandatory for both nursing and hospital staff personnel.

This is not to imply that these problems are insoluble, for they are not. Their solution requires expenditure of a considerable sum of money and, what is more important, a concerted professional effort. A real and burning desire on the part of a number of capable and industrious physicians, besides the cardiac surgeon, is prerequisite to the establishment and maintenance of a really effective cardiac surgical program. No other kind is acceptable.

Investigation

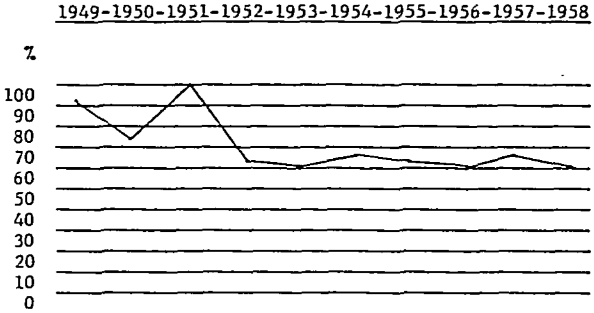
When a diagnosis of patent ductus arteriosus is made, surgery is usually recommended to the parents of the child concerned. The operative risk is discussed in terms of the mortality recorded in the surgical literature. Most available figures are those of surgeons in teaching hospitals. Since the local results do not parallel those figures, the question arises whether this is an isolated experience or representative of the results in nonteaching hospitals throughout the country. While this is often a relatively simple surgical procedure, there is surely little room for technical error. If hemorrhage does occur during surgery, it can usually be readily controlled and satisfactory therapy instituted by an experienced surgeon with a good team. In the hands of the occasional cardiac surgeon with a varying and often unfamiliar team, the result may be, and often is, tragic.

With these soul-searching thoughts in mind it was decided to undertake an investigation of the results of patent ductus arteriosus surgery in nonteaching areas throughout the United States. A questionnaire was carefully prepared for distribution to the record librarians of the largest representative civilian hospitals in nonteaching cities in all of the 50 states. In preparing the questionnaire much information was desired. Many questions were considered only to be discarded. It was recognized that the ratio of replies would be inversely proportional to the number of questions and the difficulty on the part of the busy librarian in assembling the information requested. Accordingly, questions were limited to the number of patients with patent ductus arteriosus operated on by ligation and by division, the mortality experience in each type of operation, and the number studied by cardiac catheterization and by angiocardiography preoperatively. Figures were requested for individual years from 1949 through 1958.

Every effort was made to facilitate the gathering of this information by supplying standard index numbers. A total of 448 inquiries was sent out to hospitals representing all large cities in the United States, exclusive of those containing medical schools and clinics of international renown. There were 232 returns, a response of well over 50%. The American Association of Medical Record Librarians is to be commended for the excellent cooperation on the part of its members in this study.

Report of Total Experience

The first startling information noted was that no cardiac surgery at all had been performed in 164 of the responding hospitals. This left 68 hospitals in which at least one operation had been performed for patent ductus arteriosus. The total number of patients with patent ductus arteriosus operated on in these 68 hospitals was only 508 in the 10-year period studied. This, no doubt, constitutes almost the entire experience with this type of surgery in these hospitals, since relatively few of these patients were treated outside of the teaching centers before 1949. This is an average of 7.47 surgical patients per hospital over the 10-year period, or less than one per year. This is a striking difference in volume of work between the teaching centers and these large civilian hospitals in the nonteaching localities. Since the correction of patent ductus arteriosus is usually considered one of the more elementary cardiac operations, it is reasonable to assume that this highly divergent ratio obtains throughout the entire field of cardiac surgery.. These points are worthy of note by the young cardiac surgeon. Without a good diagnostic cardiac station, it is impossible to develop a satisfactory volume of cardiac surgery. The establishment of such a station may well be the most difficult and expensive problem which he encounters.



Percentage of patients with patent ductus arteriosus treated by ligation.

Ligation or Division of Patent Ductus Arteriosus

Of the 508 operations performed, 320 (63%) were treated by ligation and only 188 (37%) by division of the patent ductus arteriosus. This is exactly the reverse of the ratio reported by Waterman and colleagues[2] in the series of 3,896 patients drawn primarily from the teaching centers. In this latter group, 63% were treated by division and 37% by ligation. Their survey covered all of the early experience before division of the patent ductus arteriosus was first proposed by Gross in 1947;[3] thus even their figures do not reflect how completely the

VARIABLE RESPONSES OF HYPERLIPEMIC PATIENTS TO ALTERED FOOD PATTERNS

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Various dietary schemes intended to reduce high serum cholesterol levels to normal have met with various degrees of success. In this study of 51 patients with elevated serum cholesterol levels, comparisons of serum lipid values were made with data from 106 normal subjects, and the effects of low-fat diets were compared with those of vegetable-oil diets. The data indicated that patients can be classified, on the basis of serum lipid fractions, into hyperglyceridemic, hypercholesteremic, and mixed types and that their responses to the diets depend on the type of abnormality present. In 9 hyperglyceridemic patients, for example, all serum lipid contents dropped to nearly normal levels with the low-fat food pattern, while in 15 hypercholesteremic patients, serum lipid levels were lower with either food pattern but did not reach normal at all. Knowledge of the patient's type of abnormality increases the likelihood of success in dietary management.

Abnormal serum cholesterol levels are most practically reduced by alteration of food patterns. Several dietary schemes have been proposed recently.[1] In a previous report[2] we described two food patterns which were effective, one sharply curtailing fat intake and the other replacing animal fat with vegetable oil. We were then primarily concerned with the design of therapeutic food patterns which would win acceptance by patients and their families. Responses to dietary treatment varied; in some patients, serum cholesterol content dropped to normal levels with either food pattern; in others, the vegetable-oil food pattern was more effective; and in a few, it remained high with either food pattern, although lower than with freely chosen foods.

Studies of the serum lipid fractions of these patients show three distinct types of hyperlipemia: hyperglyceridemia (hyperglyceridemia serves to describe a type of hyperlipemia in which triglyceride is the chief elevated fraction) and hypercholesteremia, both widely recognized types,[3] and a third which we have called "mixed hyperlipemia." More detailed descriptions of these types are given in another communication.[4] Dietary treatment was effective in patients with hyperglyceridemia and mixed hyperlipemia but relatively less effective for those with hypercholesteremia. These results suggest that the physician should know the patient's type of serum lipid abnormality in order to prescribe dietary treatment with reasonable assurance of the outcome.

Methods and Materials of Study

All blood was collected in the postabsorptive state. Serum lipid fractions,[5] lipoprotein levels, and plasma protein contents were determined before the patients began the diets and at three to six months thereafter; additional serum cholesterol levels were determined monthly. The serum lipid fractions were calculated with use of the factors recommended by the Committee on Lipid Nomenclature[5a] from determined values of total lipid,[5b] total cholesterol,[5c] free cholesterol,[5d] and phospholipid phosphorus.[5e] The triglycerides were calculated as the difference between total lipid content and the sum of free cholesterol, cholesterol esters, and phospholipid.

Description of Subjects.—This study included 51 patients with elevated serum cholesterol levels (32 men and 19 women). Forty of them were between 35 and 60 years of age and 11 between 20 and 34 years. Some form of atherosclerosis, including the various forms of heart disease, cerebral vascular disease, arteriosclerosis obliterans, and xanthomatosis, was present in 36; hyperlipemia was the only evidence of lipid abnormality in 15. Thirty-four were under dietary treatment long enough to discuss their response with reasonable assurance. The normal serum lipid values reported in this study are those for 106 employees and staff members of the Cleveland Clinic, divided equally as to sex and age range.

Abnormal Serum Lipid Types.—The three types of lipid abnormality are distinguished by different proportions of serum triglyceride, phospholipid, and free cholesterol to total serum cholesterol. Figure 1 shows averages for patients classed by type of abnormality and for normal persons. These averages were obtained from 40 patients and 53 nor-

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From the Research Division of the Cleveland Clinic Foundation and the Frank E. Bunts Educational Institute, Cleveland.

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mal subjects, aged 35 to 60 years. Similar lipid levels were present in the younger group of those aged 20 to 35 years.

Normal persons had an average serum cholesterol level of 230 mg. per 100 ml., a similar level of triglyceride, 200 mg. per 100 ml., and a higher level of phospholipid (ratio of total cholesterol to phospholipid, 0.85). Twenty-seven per cent of the total cholesterol was free.

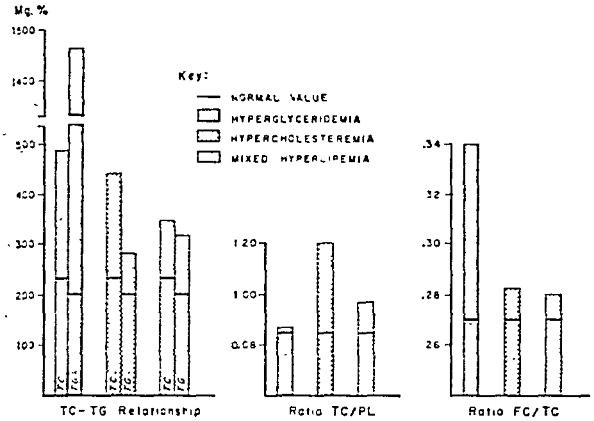

Fig. 1.—Abnormal proportion between total cholesterol (TC) and triglyceride (TG) levels in hyperglyceridemia (in which triglyceride is elevated) and in hypercholesteremia (in which cholesterol is elevated), compared to normal relationship in mixed hyperlipemia; elevated ratio between serum total cholesterol and phospholipid (TC/PL) in hypercholesteremia, compared to normal ratio in hyperglyceridemia and mixed hyperlipemia; and elevated ratio of free cholesterol (FC/TC) in hyperglyceridemia, compared to normal ratios in hypercholesteremia and mixed hyperlipemia.

In 15 hyperglyceridemic persons the average triglyceride level (1,526 mg. per 100 ml.) was three times higher than the serum cholesterol level, even though the cholesterol level was elevated to 485 mg. per 100 ml. Free cholesterol was also high, being 34% of the total cholesterol content. The phospholipid level rose equally with the level of cholesterol, so that a normal proportion was maintained. Serum lipid levels in persons within this group covered a wide range.

In 12 hypercholesteremic patients, the total serum cholesterol level was high in relation to the levels of other serum lipids; the triglyceride level was nearly normal. The average total serum cholesterol level was 436 mg. per 100 ml. and of triglyceride, 281 mg. per 100 ml. In patients with hypercholesteremia there was relatively less phospholipid than total cholesterol, the average ratio of cholesterol to phospholipid being 1.20. The percentage of total cholesterol in the free form was normal.

In 13 patients of the group with mixed hyperlipemia, the relationship between the various lipid fractions was essentially normal in spite of the elevated lipid levels. The average serum cholesterol level was 347 mg. per 100 ml., the level of triglyceride, 319 mg. per 100 ml., ratio of total cholesterol to phospholipid, 0.98, and free cholesterol, 27% of the total.

From this series of patients it is not possible to associate the incidence of any one form of atherosclerosis or xanthomatosis with a single type of serum lipid abnormality. The serum lipid values in our series confirm the sexual difference in the incidence of hyperglyceridemia and hypercholesteremia mentioned by Lever[3a] and Everett.[3b] Of 16 hyperglyceridemic patients 14 were men; 9 of 14 hypercholesteremic patients were women; and xanthelasma was present only in hypercholesteremic patients.

Changes in Serum Lipid Levels with Dietary Treatment

Thirty-four patients followed the low-fat and vegetable-oil food patterns, usually in succession, for periods sufficient to evaluate the long-term effect on serum lipid levels. The patterns and their preparation have been described previously.[2] The patients followed the low-fat food pattern for from 4 to 33 months and the vegetable-oil food pattern for from 3 to 15 months. In appraising the effect it is important to recognize other conditions which commonly alter serum cholesterol levels temporarily. Sharp drops often follow rapid weight loss, diarrhea, fever, vigorous exercise, and administration of thyroid, estrogens, nicotinic acid, or sitosterols. Serum cholesterol levels are elevated by rapid weight gain and during treatment with cortisone, testosterone, or ACTH. In this study, values affected by conditions other than diet were eliminated.

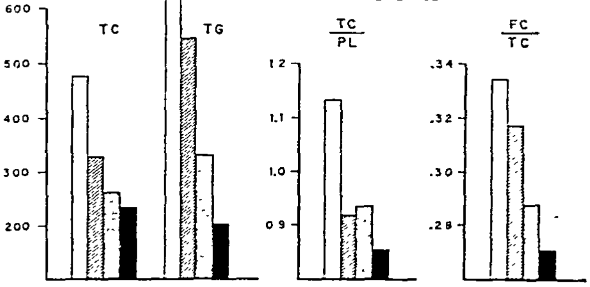

Fig. 2.—Reduction of total serum cholesterol (TC) and triglyceride (TG) levels, ratio of total cholesterol to phospholipid (TC/PL), and ratio of free to total cholesterol (FC/TC) in patient with hyperglyceridemia on freely chosen, low-fat, and vegetable-oil food patterns.

Normal Serum Lipids.—The change in serum lipid fractions in 23 normal persons was determined for two to three weeks during a dietary test in which weighed foods were served from our research kitchen. Most of these volunteers were subjects in several tests, and their individual responses to diet were verified on repetition. Both total serum cholesterol and triglyceride levels were lowered by the vegetable-oil food pattern. The ratios of total cholesterol to phospholipid and of free to total cholesterol remained within normal limits. The change in serum cholesterol level in one representative subject after three weeks on the vegetable-oil food pattern was from 240 to 170 mg. per 100 ml., ratio of total cholesterol to phospholipid from 0.93 to 0.89, and amount of free cholesterol from 25 to 27% of total.

Hyperglyceridemia.—The elevated serum lipid levels in nine hyperglyceridemic patients were reduced toward normal with the low-fat pattern. The serum lipid changes shown in figure 2 are for one patient who had been taking each food pattern for more than six months. With freely chosen foods the serum cholesterol level was 482 mg. per 100 ml. and the triglyceride level 888 mg. per 100 ml.; with the low-fat food pattern, they were 325 mg. and 545 mg. per 100 ml., respectively; and with vegetable-oil, 268 and 314 mg. per 100 ml. The ratio of total cholesterol to phospholipid dropped from 1.13 on freely chosen foods to 0.92 and 0.93 on the low-fat and vegetable-oil regimens. Free cholesterol, originally 34% of the total, was 32% on the low-fat and 29% on the vegetable-oil food pattern. A much more normal serum lipid picture was attained with the vegetable-oil than with the low-fat food pattern.

However, the vegetable-oil food pattern was not equally beneficial to all hyperglyceridemic patients. The serum triglyceride and cholesterol levels rose in two patients when they changed from low-fat to vegetable-oil food pattern, dropping to the previous level when the patients returned to the low-fat pattern.

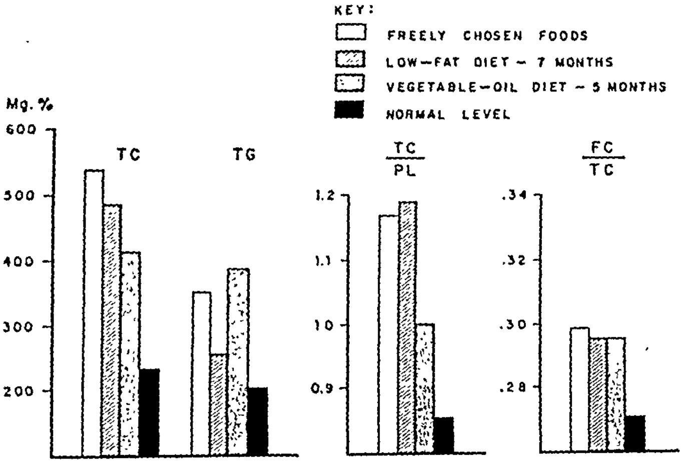

Fig. 3.—Reduction of serum total cholesterol (TC) and triglyceride (TG) levels, ratio of total cholesterol to phospholipid (TC/PL), and ratio of free to total cholesterol (FC/TC) in patient with hypercholesteremia on freely chosen, low-fat, and vegetable-oil food patterns.

Hypercholesteremia.—Hypercholesteremic subjects responded much less satisfactorily to change in food pattern than did hyperglyceridemic persons. Only 7 of the 15 hypercholesteremic patients attained normal serum cholesterol levels with either the low-fat or the vegetable-oil food pattern. The serum cholesterol level in one of these seven patients dropped from 400 mg. per 100 ml. with freely chosen foods to 375 mg. with the low-fat and 300 mg. with the vegetable-oil food pattern. The discrepancy between the serum cholesterol and phospholipid levels became less with dietary treatment, the ratio between them dropping from 1.20 to 1.12 on the low-fat and to 1.00 on the vegetable-oil food pattern.

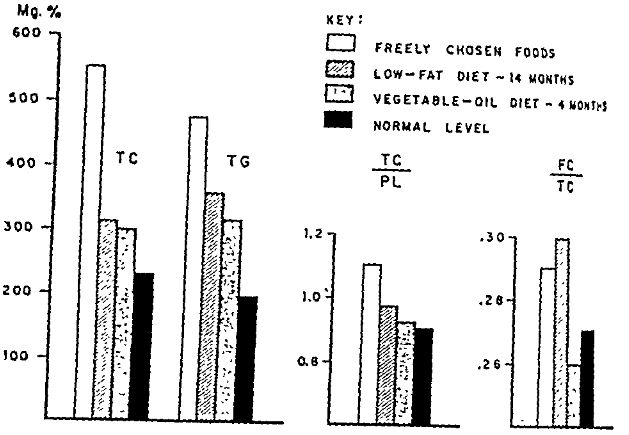

Fig. 4.—Reduction of total cholesterol (TC) and triglyceride (TG) levels, ratio of total cholesterol to phospholipid (TC/PL), and ratio of free to total cholesterol (FC/TC) in patient with mixed hyperlipemia on freely chosen, low-fat, and vegetable-oil food patterns.

Typical of the less favorable response in the other eight hypercholesteremic patients is the example given in figure 3. The serum cholesterol content dropped from an original level of 534 to 410 mg. per 100 ml. on the vegetable-oil food pattern. The abnormally high ratio of total cholesterol to phospholipid dropped from 1.20 to 1.00. In three patients in this group, the serum cholesterol level was reduced for several months with the vegetable-oil food pattern but rose thereafter without any apparent change in condition.

Mixed Hyperlipemia.—All 10 patients with mixed hyperlipemia responded to change in food pattern, their serum lipid contents dropping to normal levels and remaining stable for as long as 15 months. An example of the response of a subject whose original serum cholesterol level was the highest in this group, 548 mg. per 100 ml., is shown in figure 4.

Stability of Serum Cholesterol Levels.—The level of serum cholesterol in normal persons, eating freely chosen foods, does not vary more than ± 17 to ± 25 mg. per 100 ml. from the individual person's typical mean value. This was the variation in the yearly serum cholesterol levels of 86 normal men, 35 to 60 years of age, during a four-to-seven-year period, and in the weekly cholesterol levels of 6 women, 18 to 45 years of age, during five months. We observed the same degree of stability in patients with both hypercholesteremia and mixed hyperlipemia during 6 to 15 months of the low-fat food pattern.

In contrast, the serum cholesterol levels in hyperglyceridemic patients were quite variable. When neither food nor weight was controlled, the level changed several hundred milligrams in some patients in a month's time. With the low-fat food pattern it varied ± 25 to ± 53 mg. per 100 ml. over a period of 6 to 12 months. Differences with weight fluctuations were marked in hyperglyceridemic but negligible in hypercholesteremic patients.

A change from low-fat to vegetable-oil food pattern produced a more stable serum cholesterol level in almost all patients, regardless of their abnormal lipid type. This was especially notable in hyperglyceridemic patients. For example, the serum cholesterol level in one representative patient varied ± 53 mg. per 100 ml. during a year of the low-fat food pattern and only ± 15 mg. per 100 ml. in a year of the vegetable-oil pattern.

Comment

"Hyperglyceridemia" is chosen to describe the condition previously called hyperlipemia. We would like to recommend its general use because the term indicates the specific lipid fraction, triglyceride, which is disproportionately elevated. In the same way, the accepted term hypercholesteremia describes the disproportionate elevation of serum cholesterol content. Hyperlipemia can then be used as the general term for all elevations of serum lipid content. A hyperlipemic person is one with elevated lipid fractions, requiring further classification as to the type of abnormality, whether hyperglyceridemia, hypercholesteremia, or mixed hyperlipemia.

Both hyperglyceridemia and hypercholesteremia have been recognized and described adequately.[7] We found, however, that 35% (18 of 51) of the patients under study whose serum lipid fractions were determined did not conform to either of the two types of abnormality. These persons fitted better into a third classification, which we have called "mixed hyperlipemia" because features of both of the other hyperlipemias were present. This type is probably the one described by Gofman [6] which has "across the board" elevations of lipoproteins. The distinguishing characteristic of the serum lipid levels in this group is their normal relationship to one another despite their elevation. Mixed hyperlipemia is distinguished not only by chemical lipid fractions but also by a lipoprotein pattern [4] in which all classes of the —S 1.21 beta lipoproteins (—S 70-400, 40-70, and 25-40) are high. In contrast, the —S 25-40 fraction is normal in hyperglyceridemia and —S 70-400 fraction is normal in hypercholesteremia. Mixed hyperlipemia may not have been generally recognized before, because the determination of serum lipids has only recently become a diagnostic practice.

Decision concerning the type of normal lipid pattern present in a patient requires analysis of a fasting blood sample after at least three weeks of habitual foods with none of the conditions overtly affecting serum lipid levels being present. Classification of abnormal lipid types does not require knowledge of the complete lipoprotein and lipid fractions. Values for total and esterified cholesterol and for lipid phosphorus afford a sufficient basis for most diagnoses. These determinations are usually available in clinical laboratories. The triglyceride level may be an added help but is not essential.

Hyperglyceridemia can usually be recognized by the milky appearance of the patient's fasting serum sample. A high ratio of free to total cholesterol confirms this finding even if the total cholesterol level is normal. A hypercholesteremic patient can usually be recognized by a high ratio of total cholesterol to phospholipid. A normal ratio of free to total cholesterol confirms the diagnosis, as does a normal triglyceride level. High serum cholesterol levels, with a ratio of total cholesterol to phospholipid usually no more than 1.05 and a normal ratio of free to total cholesterol, confirms the classification of mixed hyperlipemia.

There is some overlapping in the ranges of lipid values for the occasional patient with slightly elevated serum lipid levels. Visible lipemia may not always be present in a patient with hyperglyceridemia because of temporary reduction of serum lipid levels. For lactescence, the neutral fat content must be above 600 mg. per 100 ml. (20 mEq. of neutral fatty acids).[8] For such patients the lipoprotein pattern is needed for proper classification.

Recognition of the three types of hyperlipemia is necessary for an understanding of the response to dietary treatment. While high lipid levels become reduced in most patients with proper food patterns, the extent of the change differs. Instability of the serum cholesterol level in hyperglyceridemic patients may be responsible for changes while the patient is taking a low-fat regimen, rather than the patient's failure to follow the food pattern. If the patient is warned that his cholesterol level will vary, he is saved from discouragement and continues with the food pattern with better will. The hyperglyceridemic patient maintains a steadier serum cholesterol level with the vegetable-oil than with the low-fat food pattern. This probably would be the better diet for such patients, except those whose serum cholesterol levels rise if they eat any kind of fat.

Only partial reduction of serum lipid levels can be achieved by dietary treatment of hypercholesteremic patients. Although their serum cholesterol levels are reduced with either low-fat or vegetable-oil regimens, they may not reach normal values. The characteristic of high cholesterol levels of this type is their resistance to change with weight fluctuation. Patients should be told in advance that they are better off with the food pattern than they would be freely choosing their foods but that dietary treatment probably will not bring their serum cholesterol level down to normal.

The elevated serum cholesterol level of the patient with mixed hyperlipemia responds readily to either the low-fat or vegetable-oil food pattern, dropping to normal levels and remaining there.

Other elevated lipid constituents, such as phospholipids, triglycerides, and esterified cholesterol, respond similarly to dietary treatment, but not to the same extent. Although serum cholesterol levels may be normal, the lipoprotein fractions may still be elevated.[4] When dietary treatment is fully successful in reducing the serum cholesterol level in a patient with any of the three abnormal lipid types, the levels and relationships of the serum lipids tend to approach the normal range.

Some may not respond to dietary treatment because of their previous food selection. Persons who normally choose low-fat foods or have attempted dietary restrictions before following the more rigidly controlled food patterns may show only a small drop in serum lipid levels.

Summary

Studies of the serum lipid fractions of 51 patients with high serum cholesterol levels show three distinct types of hyperlipemia, (*a*) hyperglyceridemia, in which the triglyceride fraction is high relative to the cholesterol level, the ratio of cholesterol to phospholipid is normal, and the ratio of free to total cholesterol is high; (*b*) hypercholesteremia, in which the cholesterol level is elevated in relation to the nearly normal triglyceride level, the ratio of cholesterol to phospholipid is high, and the ratio of free to total cholesterol is normal; and (*c*) mixed hyperlipemia, in which all serum lipid levels are elevated but are in normal proportions to each other.

Two years' experience with the effect of low-fat and vegetable-oil food patterns on the serum lipid levels of 34 of these 51 patients show that their abnormal serum lipid levels responded to dietary treatment according to the type of abnormality present. In nine hyperglyceridemic patients, all serum lipid contents dropped to nearly normal levels with the low-fat food pattern, yet the triglyceride levels were still high relative to the cholesterol. The highly variable serum cholesterol level became not only low but much more stable with the vegetable-oil than with the low-fat food pattern. However, two hyperglyceridemic patients had higher serum cholesterol levels with the vegetable-oil than with the low-fat food pattern.

In 15 hypercholesteremic patients, serum lipid levels were lower on either food pattern but di not reach normal in all. In eight the serum cho lesterol level did not fall below 350 mg. per 100 ml In 10 patients with mixed hyperlipemia serum lipi contents dropped readily and remained at norma levels. These results suggest that the physician wit knowledge of the patient's type of serum lipi abnormality may prescribe dietary treatment wit reasonable assurance of the outcome.

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CLINICAL NOTES

SEPTIC THROMBOPHLEBITIS DUE TO A SPECIES OF ACHROMOBACTER IN A FOUR-YEAR-OLD BOY

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The occurrence of high fever in an otherwise well child, a day or two after operation, leads the experienced surgeon to throw back the sheets and look for a saphenous phlebitis at the site of a cutdown. The child is usually not particularly ill, although there is generally a visible erythema, tenderness, induration along the course of the vein, and frequently edema of the leg. Blood cultures made by ordinary methods are generally sterile. The condition responds at once to withdrawal of the intravenous cannula, polyethylene catheter, or indwelling needle and local application of hot compresses. The plastic indwelling catheters have become particularly popular and have led to the more frequent use of continuous intravenous drips.

A number of reports have appeared listing the hazards and complications which result from use of this technique.[1] Septic thrombophlebitis is probably the most serious complication and has led to bacteremia and septicemia, profound illness, protracted hospitalization, and, on some occasions, death.[2] The incidence of this hazard increases with the length of time that the intravenous catheter is left in place. While the possibility of phlebitis occurring after either an open or blind insertion of the cannula is well known, it may not be appreciated that the same sequence of events may follow after use of an indwelling needle. Pediatricians particularly have become exceedingly adept at placing needles in small veins of the extremities or scalp and strapping them in place so that fluids may at times be given for several days through one such vena puncture.

Report of a Case

A 4-year-old boy was admitted to the hospital with a history of abdominal pain of one week's duration. He had tenderness, muscle spasm, and rebound tenderness referred to the right lower quadrant; it was thought that he had appendicitis. Operation revealed a perforated Meckel's diverticulum with an abscess at its tip, the whole enveloped by omentum. The diverticulum was resected and the intestine closed, the diverticulum and the intact omentum surrounding the abscess being removed from one specimen. Culture of the abscess cavity revealed a mixed infection from which there grew out Escherichia coli, alpha hemolytic enterococci, diphtheroids, Escherichia freundii, and beta streptococcus, not group A.

The boy had an initially smooth course. His temperature, which had risen to 102 F (38.9 C) rectally immediately after operation, dropped to normal on the second day and remained there until the fifth day after operation. On that day his temperature suddenly rose to 105.2 F (40.6 C). The abdomen was soft and flat. There were good bowel sounds and the boy did not appear particularly ill. He had been receiving penicillin and streptomycin, and chloramphenicol (Chloromycetin) was now added to the regimen. The next day a blood culture, taken at the time of the temperature spike, was reported to show a luxuriant growth of a species of Achromobacter. The exact species was not identified. These are normally soil organisms and nonpathogenic. The next day repeat blood cultures revealed the same heavy growth of an Achromobacter species; this was taken as the explanation for the boy's fever, as the abdomen continued to be soft and he was taking fluids by mouth and passing stools easily.

Cultures of the organism were resistant to all of the conventional antibiotics but sensitive to kanamycin sulfate (Kantrex). On the seventh postoperative day, 50 mg. of kanamycin was given four times daily in addition to chloramphenicol; use of penicillin and streptomycin was discontinued. On the seventh day the patient's temperature rose to 102 F, and on the eighth day, to 103 F (39.4 C). At this time one of us noted a small area of discoloration over the radial aspect of the right wrist (see figure). There was an obvious area of pressure necrosis over the radius with a little erythema and edema surrounding it. It seemed obvious that the hub of the needle had been strapped so firmly to the wrist that it caused this small 0.5-by-2.0 cm. area of skin necrosis. From this point proximally one could see and feel a firm cord, obviously representing the thrombosed cephalic vein. The thrombosed vein could be traced as far as the middle of the

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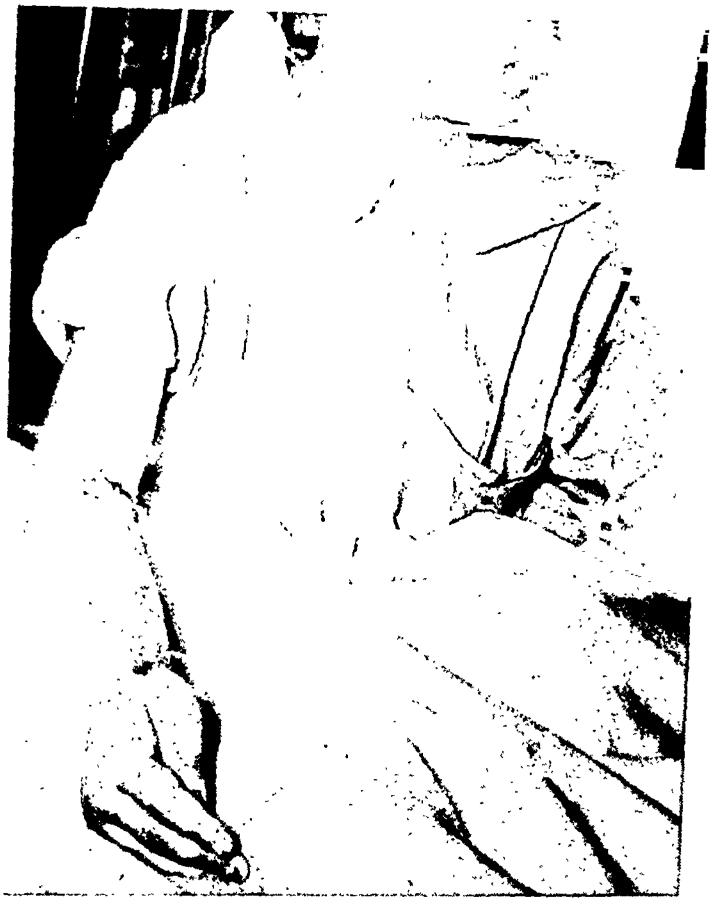
forearm. It seemed possible that this represented a septic thrombophlebitis, the source of the patient's bacteremia.

Culture of the little wound at the wrist yielded Achromobacter species. However, before these results were known, a small incision was made with local anesthesia in the antecubital fossa, the cephalic vein was ligated and divided, and a portion of the vein was taken for culture. Simultaneously a blood culture was taken from the opposite forearm. Both of these cultures yielded heavy growths of Achromobacter. One hour later another blood culture was taken from the femoral vein and was negative. Blood cultures taken for each of the next two days were similarly negative.



Patient shortly after ligation and division of cephalic vein in antecubital fossa. On radial aspect of wrist one can see shape and size of area of necrosis and surrounding erythema resulting from tight strapping of needle to wrist. Thrombosed vein was palpable as tender cord extending from discolored area half way up forearm.

In the 12 hours after the division of the vein, the boy's temperature dropped from 103 F to 98 F (36.7 C) and remained normal. The small area on the wrist healed promptly. The kanamycin and chloramphenicol were nevertheless given until the 13th day after the laparotomy. Although the boy's condition, objectively viewed, had never presented cause for alarm, he had been ill, "washed out," and listless.

Comment

Although a portion of the thrombus was not removed for the study, the evidence was conclusive that we were dealing with a septic thrombophlebitis of the cephalic vein. Presumably this was initiate as a bland process accompanying the initial infusion. Investigation of the circumstances of thi infusion indicated that the needle probably ha been strapped in place for at least 24 hours. Th thrombophlebitis per se would ordinarily not hav led to septicemia. Pressure from the hub of th needle in the skin directly over a portion of th vein produced necrosis and a portal for entry the very unusual organism which ultimately infected the clot within the vein.

In aseptic thrombophlebitis, which often accompanies intravenous infusions, the clot forms withi the vein, gradually organizes, and ultimately becomes fibrous, particularly when hypertonic solutions are given. There is little danger to be anticipated from such thrombosis of superficial vein either in the upper or lower extremities. Suc thrombi rarely extend into the major vessels break off to serve as a source for emboli. If infectio of the clot supervenes, however, the situation immediately changed. Organization of the bacteri harboring thrombus is interfered with, and embo are flicked off into the blood stream from the crumbling friable mass. In this instance no petechii wer seen. Although the establishment of secondary fo of infection may be prevented initially by the use antibiotics, the clot continues to support the growt of the organisms protected in this favorable situatio With the passage of time the organisms becom resistant to one after another of the antibioti used, until the septicemia overwhelms the patien If the source of the infected emboli can be foun simple ligation, ligation and division of the vein, excision of the thrombus or thrombotic segment wi be a curative measure. The remaining infectio usually of low grade, trapped in the isolated segment of vein and no longer feeding into the circulation, will generally resolve.

Summary

Septic thrombophlebitis of the cephalic vein due to a species of Achromobacter developed in a 4-year-old boy. The hub of a needle inserted into the cephalic vein at the wrist had been tightly strapped to the skin for about 24 hours. Local pressure necrosis at the site of the needle hub provided a point of entry. Ligation and division of the cephalic vein in the antecubital space led to prompt recovery and immediate disappearance of the organisms from the blood stream.

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ANAPHYLACTOID REACTION TO INGESTION OF ORANGE

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The ingestion of fruits is known to cause urticaria, diarrhea, angioneurotic edema, palatal itching, migraine, allergic rhinitis, asthma, and rarely, purpura. A search through the literature failed to reveal any previously observed case of anaphylactoid shock due to ingestion of an orange. Our experience with such a case prompted this report.

Report of a Case

A 48-year-old woman was seen in the emergency room of Hahnemann Medical College and Hospital at 4:30 p. m. on March 25, 1959, complaining of dizziness and a diffuse skin rash. She had eaten a fresh orange at noon on that day. By 3 p. m. she had developed itching at the neck and malaise. She left her job at a textile mill and shortly thereafter felt dizzy, thirsty, and chilly and was brought to the emergency room in shock. She stated that all other foods eaten on that day had been eaten frequently recently, without reaction, and that she had not been in contact with any new substance at her job or at home. She had eaten neither oranges nor any foods containing orange for two years prior to this day of admission. Two years earlier she had eaten a fresh orange and developed a pruritic skin eruption associated with generalized swelling, but no dizziness or vomiting, and had sought no medical care at that time. She had not consumed wine the week prior to admission. The family history revealed that the patient's father and one brother had asthma. The patient's medical history was otherwise unremarkable for allergies, including contact sensitivity to textiles. She claimed to have eaten oranges all her life without consequence prior to the episode two years previously.

Physical examination revealed a moderately obese, restless woman whose skin was covered with large urticarial lesions. The blood pressure, which was initially 70/40 mm. Hg, became much less perceptible within two to three minutes; the pulse was 120 per minute and the respiratory rate 26 per minute. Temperature was 98.6 F (37 C). She was thirsty, had shaking chills, and required several blankets to comfort her sensation of cold. The upper lip was edematous. Ausculation and percussion of the lungs revealed no abnormality. The apical rate was 120 per minute, and frequent premature systoles were heard. No masses or tenderness were noted in the abdomen, and bowel sounds were normal. Findings of a neurological examination were normal. There was a generalized urticarial eruption, most prominent over the trunk and thighs.

Treatment and Recovery.—A diagnosis of acute allergic reaction, with shock due to ingestion of an orange, was made and treatment instituted with intravenous administration of 0.3 cc. of a 1:1,000 solution of epinephrine. Metaraminol (Aramine) bitartrate, 25 mg., was given directly intravenously, followed by an intravenous infusion of 25 mg. of metaraminol and 100 mg. of hydrocortisone in 500 cc. of 5% glucose in water, with a gradual response in blood pressure, which was maintained at 120/80 mm. Hg with slow infusion of this solution. Parenterally given tripellenamine (Pyribenzamine) hydrochloride, 25 mg., was also administered. The itching and urticaria began to subside and were almost completely resolved within three hours after admission. The metaraminol infusion had to be continued for six hours, during which time, for brief intervals, the blood pressure slowly dropped on repeated attempts to terminate the use of this vasopressor drug.

On discharge, eight hours after admission, the patient's blood pressure was stable at 120/70 mm. Hg, without administration of any medicament, and the urticaria and itching had disappeared although there was still mild edema of the upper lip. Auscultation of the heart at this time failed to reveal any abnormal rhythm, and electrocardiographic findings were normal.

Results of laboratory studies were as follows: hemoglobin level, 12.2 Gm.%; hematocrit reading 41%, total white blood cell count 6,500 per cubic millimeter, with a differential count of 65 polymorphonuclear cells, 35 lymphocytes, 7 monocytes, and 2 eosinophils per 100 cells counted. The urine was amber-colored and cloudy, contained no sugar, acetone, or protein, and on microscopic examination showed 3 to 5 red blood cells and 10 to 15 white blood cells per high-power field; no casts were present.

The patient was seen 24 hours after her recovery; she was asymptomatic and had a blood pressure of 120/70 mm. Hg. Intradermal skin tests (see the figure) revealed a positive reaction to freshly extracted, undiluted orange juice (obtained by needle puncture of an orange) and negative reactions to standard stock orange extracts, diluted orange juice prepared six hours previously, and scratch testing to all these preparations. No pseudopodia were seen in the positive reactions. She exhibited no harmful or anaphylactoid response to the skin-testing stimulus. Six patients used as controls failed to manifest a positive skin reaction to the fresh orange juice. A sample of the patient's serum was obtained at this time, and a Prausnitz-Küstner

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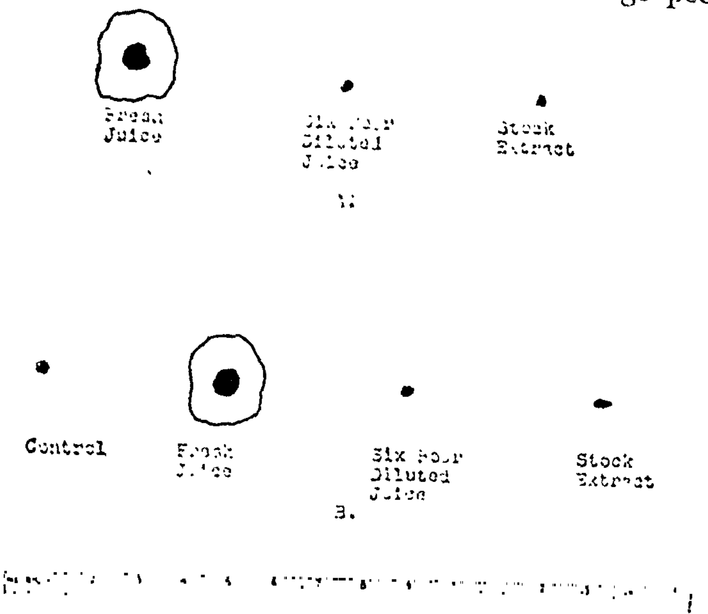
passive transfer test was also performed on a nonallergic subject who had abstained from oranges or orange products for 48 hours. Again, a positive reaction was obtained only with intradermal injection of the fresh orange juice and not with the stock extracts.

Comment

Many cases of presumed "allergy to orange" are no longer considered true cases of allergy but instances of gastric irritation due to orange peel oil or, in cases of "peeler's dermatitis" in industry, they are nonallergic contacts with the primary irritant in the oil.[1] Furthermore, the studies of Ratner and associates[1] suggested that orange juice protein does not appear to traverse the gastrointestinal wall readily even when ingested in large amounts.



Intradermal tests with orange juice allergen. *A*, direct skin tests on patient. Filled-in area represents induration; outside circle represents extent of erythema. *B*, passive transfers with patient's serum. Control represents introduction of allergen in unprepared skin of nonallergic subject.

Actual cases of allergic reactions to oranges are well recognized,[2] with manifestations of chronic urticaria, allergic coryza, and asthma. Ratner and associates[3] showed that fresh orange contains two distinct allergens, one in the seed and the other in the juice itself, the latter being much less potent than the seed protein. The severity of the reactio observed in the case described might suggest tha the offending allergen was more likely to be th seed protein; we have no reason, however, t believe that the patient ingested any seeds and therefore must attribute the reaction to the juice allergen.

The observation that positive reactions to skin tests were obtained only with fresh orange juice and not with stock extracts, tends to corroborate the findings of Tuft and associates,[4] who demonstrated the presence in food extracts of a labile factor which deteriorates with time and therefore results in the large percentage of negative results of skin tests for food allergies. Kahn[2] had previously reported that typical pseudopodic wheals are rare.

Summary

A case of allergy to orange juice occurred late in life in a patient exhibiting urticaria, angioneurotic edema, shock, frequent premature cardiac beats, positive reaction to skin tests for fresh orange, and successful passive transfer. This is the first such reported example of anaphylactoid shock from ingestion of an orange.

The optimum method for confirmation of sensitivity to fruit allergen includes the use of intradermally administered fresh material. The intradermal wheal need not have pseudopod formation. Therapy with metaraminol (Aramine) bitartrate was successful in maintaining normotensive levels of blood pressure during the recovery phase in this patient's anaphylactoid shock.

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DIETARY MANAGEMENT OF MULTIPLE SCLEROSIS.—Patients with multiple sclerosis have been observed on a low-fat diet for a period of nine and a half years. The frequency and severity of exacerbations in all cases were significantly reduced, and the performance of patients first treated in the early phase of the disease was improved or unaltered during this period. In the intermediate- or late-phase patients, the course of the disease was less dramatically improved. It appears that if the low-fat diet is instituted early and adhered to carefully, the course of the disease is significantly improved.—J. H. Schulte, M.C., U. S. Navy, Feeding Problems in the Submarine Service, *Journal of the American Dietetic Association*, April, 1960.

CLINICAL SCIENCE

PYELONEPHRITIS

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Interest in pyelonephritis and its consequences [1] appears to have been increasing in recent years. Although fundamental contributions to our knowledge of this disorder were made in previous decades, the recent quantitative investigations of the normal and pathogenic bacteriology of the genitourinary tract appear to be a major stimulus for this growing interest. The magnitude of the problem is emphasized by the finding that the incidence of chronic pyelonephritis in autopsy material from many series varies from about 10 to 20%. In recent studies of 629 cases of pyelonephritis found at autopsy, only 104 of these had been diagnosed prior to death. This indicates the lack of knowledge on the part of the physician of the varied clinical picture of the disease and the failure to interpret significant laboratory findings as indicative of urinary tract infection.

Pathogenesis of Pyelonephritis

The pathogenesis of pyelonephritis can be discussed from both the clinical and experimental standpoints. Attempts have been made to evaluate the role of lymphatic channels, hematogenous spread, and ascending infection. While there is little evidence to support the concept of spread of infection from the lower urinary tract to the kidneys via the lymphatics, arguments can be marshaled in favor of the hematogenous and ascending pathways. Evidence for the hematogenous route may be seen in the occurrence of staphylococcic abscesses in the kidneys of patients with an obvious distant focus. The evidence which supports the concept of the ascending route of infection is summarized as follows:

First, pyelonephritis occurs much more frequently in women than in men, except in the older age groups. It has been postulated that this is due to the fact that the female urethra is shorter and more liable to contamination.

Second, cystitis occurs in a high percentage of patients after single catheterization, and the incidence is higher when indwelling catheters are used. It has been shown that the bacteria enter the bladder along the mucopurulent sheath which forms between the urethral mucosa and the outer catheter wall.

The importance of instrumentation in the iatrogenic spread of urinary tract infections and its role in initiating the sequence of events leading to ascending spread can be seen from the following examples: 1. The high incidence of infection in patients with neurological disease and associated bladder disturbances is related to the insertion of a catheter. At the time of initial instrumentation, the urine obtained is usually sterile but urethritis and cystitis ultimately develop. 2. Although obstructive disease of the urinary tract predisposes the kidney to infection, it has been established that pyelonephritis is more frequently seen when lower rather than upper urinary tract obstruction is present. This finding has been correlated with the greater incidence of catheterization in the former group. 3. Studies of the incidence and pathogenesis of hospital-acquired urinary tract infections have indicated that transmission occurs via the contamination of catheters by ward personnel. 4. In an analysis of nosocomial gram-negative bacterial infections, it has been demonstrated that antibiotic-sensitive organisms were isolated from the urine of patients who showed evidence of acute urinary tract infection before hospitalization and in whom catheterization was infrequent. In those with antibiotic-resistant bacteria there was a high correlation with recent instrumentation or catheterization.

How frequently ascent of infection occurs via the ureter (lumen or wall) as compared to the hematogenous dissemination of bacteria cannot be determined but obviously depends on such variables as the age and sex of the population examined, the presence or absence of catheterization, associated uropathies, and distant foci of infection.

The factors which predispose the kidney to infection may be considered under the categories of (1) congenital developmental factors and (2) acquired factors. Such congenital developmental factors as aplasia, hypoplasia of varying degrees, "focal dysplasia," cystic disorders of the kidney, and horseshoe kidney are associated with a higher incidence of infection than is found in the normal kidney. The exact role by which these renal de-

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fects predispose to infection is not clear, but certain observations suggest that these lesions, whether generalized or focal, constitute an area of "tissue inferiority" or locus minoris resistentiae.

Acquired factors which predispose the kidney to infection include obstructive lesions of the urinary tract. Obstruction to the flow of urine has long been appreciated as an important finding in the pathogenesis of pyelonephritis. It is apparent that obstruction at the level of the nephron, as well as at any place along the urinary tract up to the urethral meatus can exert this influence. It is important to understand that "functional obstruction" can occur in the absence of mechanical lesions. The mechanisms by which urinary obstruction renders the kidney more susceptible to infection are unknown.

Other acquired factors which may play a role in the pathogenesis of urinary tract infections are gout, nephrocalcinosis, potassium deficiency, and vitamin A deficiency. While the metabolic disorders in these conditions are dissimilar, the basic mechanism by which they appear to predispose to infection is the common finding of tubular obstruction and internal hydronephrosis.

Urethral instrumentation must be stressed as an acquired factor in producing urinary tract infection. There is a large body of published data which appears to support this contention. With the availability of the technique of quantitative urine cultures, the use of the catheter to obtain urine for diagnostic purposes is rarely necessary. Clean, voided specimens are adequate for this purpose. The decision to use an indwelling catheter must be made with caution and understanding of the risks involved. If catheterization is performed, bladder irrigation with 0.25% acetic acid or some similar antibacterial agent should be instituted.

Immunological factors in the pathogenesis of pyelonephritis have received little attention in the literature. Although it has been suggested that these mechanisms may be operative, there have been few attempts to demonstrate them. Further work in this area is needed. Studies of the pathogenesis of experimental pyelonephritis have been limited because of a lack of a suitable model. Although such factors as ureteral obstruction, mechanical trauma, localized injury to the medulla, preceding staphylococcic infection with resultant scarring, and desoxycorticosteroneacetate-induced arteriosclerosis will predispose the kidneys of experimental animals to pyelonephritis, the investigator is frequently unable to distinguish between the effects of the predisposing injury and the induced infection. The intravenous injection of certain strains of Streptococcus faecalis into normal rats results in acute pyogenic infection of the kidney. This infection is characterized by the persistence of bacteria in relatively constant numbers during the evolution of the disease from the acute to the chronic stage. It is of interest that hypertension was not noted in the chronic enterococcic pyelonephritis in the rat. This experience is in keeping with the findings reported in the literature by other investigators on the lack of occurrence of hypertension in experimental kidney infections. This has been attributed to the almost universal failure to demonstrate the finding of arteriolar lesions in experimental pyelonephritis. In this respect it should be remembered that attempts to correlate animal experimentation with human disease are of only limited value.

Pathological Picture

The pathological changes within the kidney in clinical and experimental pyelonephritis are strikingly similar. There is one important difference, however. The human disease is characterized by a high incidence of vascular changes in the area of acute and chronic inflammation. They vary from acute arteritis, including the complete occlusion of major arteries within the kidney, to the characteristic proliferative endarteritis which resembles the hyperplastic arteriolosclerosis that accompanies malignant nephrosclerosis and is present in the most extensively scarred areas. As mentioned above, no significant vascular lesions have been conclusively demonstrated in any experimental preparation of acute or chronic pyelonephritis. This may account for the striking difference in the incidence of hypertension in human and experimental studies.

The hallmark of a pyelonephritic kidney is the complexity and pleomorphism of the pathological picture. Many functional studies which use techniques that measure renal hemodynamics and maximum tubular reabsorptive and excretory capacities suggest that the remaining functioning nephrons are normal; that is, despite the extremely pleomorphic character of the histological picture, a pleomorphic functional pattern is not observed. This strongly suggests that a great deal of the abnormal structure observed histologically is viable but does not contribute to the excretory function of the diseased kidney. This may be characteristic of many types of severe chronic renal disease. Certain functional alterations, however, appear more commonly in the chronic pyelonephritic than in the chronic glomerulonephritic or nephrosclerotic kidney. Between 1956 and 1958, we observed 55 hospitalized patients with chronic pyelonephritis who had varying degrees of azotemia (serum creatinine level of 3 to 30 mg. %). Nineteen of these patients demonstrated a distinct defect in the renal conservation of sodium, which occasionally reached proportions consistent with so-called salt-losing nephritis. By contrast, during the same period, only 4 of about 40 patients with chronic glomerulonephritis who had comparable degrees of azotemia showed any defect in sodium conservation, and these were seen only with the severe degrees of renal damage (creatinine level higher than 7 to 8 mg. %). These data confirm the observations in the literature that a clinically significant defect in sodium conservation occurs more frequently in chronic pyelonephritis than in chronic glomerulonephritis.

Progressive impairment of the concentration and dilution capacities of the kidney are seen in all forms of progressive destruction of the renal parenchyma. Two characteristics of the pyelonephritic kidney were noted, however, that have not been observed in the chronic glomerulonephritic or nephrosclerotic kidney, namely, (1) the occasional presence of a serious concentration defect at a serum creatinine level below 2 mg. %, and (2) the presence of a concentration defect manifested by the inability to concentrate the urine even to isotonicity, despite dehydration or administration of vasopressin (Pitressin). In other words, these patients are persistently hyposthenuric. This type of functional aberration has been called "acquired nephrogenic diabetes insipidus." The tubular abnormality resulting in hyperchloremic acidosis is almost characteristic of the chronic pyelonephritic kidney. Presence of this type of acidosis in a chronic, acquired renal disease, in which a congenital tubular lesion seems ruled out, suggests the diagnosis of chronic pyelonephritis.

Clinical Picture

The clinical picture of acute and chronic pyelonephritis may be as pleomorphic as that of the pathological findings. Unfortunately, years may pass during which the patient is totally unaware of the continuing effects of the suppurative process within his renal parenchyma. Significant symptoms may appear only when the patient has developed renal insufficiency or severe hypertensive disease. At this time, if a meticulous medical history is taken, one may obtain information referable to previous catheterization, abnormal urinary sediment, and cystitis treated without follow-up. It is distressing to realize that many patients in this group have had abnormalities in their urinary sediment brought to their attention but have done nothing to correct it.

The acute picture of pyelonephritis, particularly in the older age group, may be characterized by a minimum of urinary symptoms and flank pain, the presence of only intermittent low-grade fever, and gastrointestinal complaints and ileus. Every author writing about acute pyelonephritis stresses the fact that random urine specimens may be free of leukocytes, casts, or red blood cells. If the fresh urinary sediment is examined daily during the acute process of the disease, one cannot fail to be impressed by the intermittent nature of the pyuria. Certainly, the diagnosis of acute pyelonephritis should not be excluded when one or two urine specimens are normal. The "silent" nature of the chronic disease in the face of continuing bacteriuria indicates the need for and importance of quantitative urinary cultures in the definitive diagnosis of pyelonephritis. One recent study has indicated that significant bacteriuria is present in at least 20% of hospitalized patients with or without symptoms referable to the urinary tract.

The demonstration of significant bacteriuria as opposed to bacteriuria consistent with urethral contamination is the most important index of the diagnosis of urinary tract infection, bearing in mind the inability to distinguish, with bacteriological methods, between upper and lower urinary tract infection. In patients with acute or chronic pyelonephritis who have not been submitted to urinary tract manipulation, Escherichia coli and closely related coliform bacteria predominate in contrast with the more resistant bacteria, such as Aerobacteraerogenes, Proteus, Pseudomonas, and staphylococci, which greatly increase after these procedures. When simple quantitative methods which may require culture of only a 10^{-3} dilution of urine are used, it can be said with confidence that patients with 100,000 bacteria or more per milliliter of urine have "significant bacteriuria," even in the absence of symptoms or other urinary evidence of infection.

Chemotherapy

The variety of antibacterial agents available for control of bacteriuria is exceeded only by the varied statements concerning their success, depending particularly on the character of the case material studied and the care supplied by and duration of follow-up after treatment. Administration of agents to which the bacteria in the urine are sensitive is generally followed by good immediate results without any clear superiority of one agent over the other. If the period of follow-up after treatment is sufficiently prolonged, the relapse rate appears more related to the nature of the disease than the chemotherapeutic agent employed. The clinical response of the patient can neither determine the cure of infection nor the value of the chemotherapeutic agent; rather, the results of treatment must be considered in terms of immediate as well as long-term urinary sterilization. The factors which particularly influence the results of chemotherapy in an unfavorable fashion are (1) interference with the free flow of urine at any point in the urinary tract and (2) a history of recurrent episodes of urinary infection.

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THE JOURNAL
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PAROXYSMAL NOCTURNAL HEMOGLOBINURIA

SLIGHTLY more than 200 cases of paroxysmal nocturnal hemoglobinuria (PNH) have been reported; yet numerous articles have appeared concerning the pathogenesis of this disease. Although the basic abnormality in PNH resides in the red blood cells, hemolysis in PNH depends on a complex hemolytic system present in both PNH and normal plasma. The observation by van den Bergh [1] in 1911 of peculiar susceptibility to hemolysis in PNH on acidification of the serum remains the point of departure for further investigation and is the basis of the acid hemolysin test of Ham. Critical concentrations of magnesium and calcium are essential for optimum hemolysis, as is the presence of complement or "complement-like" factors. The demonstration by Crosby that preparations of thrombin enhance hemolysis in PNH is the basis for an additional diagnostic test as well as for further study of the plasma hemolytic system. The attempt to attribute the "thrombin effect" to contamination with properidin has been refuted and retracted.[2] There exists no over-all agreement among investigators as to whether preparations of thrombin enhance PNH hemolysis by virtue of thrombic activity per se or contamination either with heterophil or iso-antibodies [2b] or other as yet unidentified substances.

Crosby [3] suggested that the plasma system consists of two hemolytic factors and two inhibitors related to the blood coagulation mechanism. These factors have not been identified. Despite frequent thrombocytopenia in PNH, thrombosis occurs rather than hemorrhage. No precise information exists which permits the correlation of the in vivo tendency to thrombosis with the fact that in vitro hemolysis can be augmented by accelerated blood coagulation. Further studies on PNH may shed light on the pathogenesis of thrombosis in general.

Although many substances inhibit the activity of the PNH plasma hemolytic system in vitro,[4] there are distinct limitations to the use of such agents therapeutically. In vitro studies suggest that only a small proportion of PNH cells are "sensitive" to the plasma hemolytic system at any given time and that in vivo hemolysis proceeds at a relatively slow but steady rate. Inhibition of the plasma hemolytic system permits an accumulation of these "sensitive" red blood cells. If the suppressing agent is withdrawn or loses its effectiveness, a severe "rebound" hemolysis may occur. Similarly, chronic low-grade hemolysis may maintain the various plasma hemolytic factors at relatively low concentrations. Because normal plasma contains hemolytic factors, washed red blood cells, instead of whole blood, are preferable for transfusion.

Study of the biochemical defect of the PNH red blood cell should provide a fundamental approach. The defect is thought to reside in the stromal fabric. No abnormality in hemoglobin or in osmotic or mechanical fragilities has been detected. Unusual susceptibility to a variety of erythrocyte heterophil and iso-antibodies has been attributed to an abnormality in the "antibody receptors" on the PNH erythrocyte surface, but no erythrocyte antibody has been demonstrated in uncomplicated cases of PNH. Electron microscopy has revealed a patchy and pitted PNH erythrocyte stroma. Abnormality in fatty acid composition has been reported.[5] Significant differences from normal in stromal phospholipid pattern have been both claimed and denied.[6]

It has been suggested that the PNH erythrocyte is defective in surface enzyme systems which preserve and renew the stromal fabric.[4] Marked impairment of erythrocyte acetylcholinesterase activity (AChE) has been noted [7] in 12 of 14 PNH cases in one study, and in 6 of 7 cases in another. Of the two patients with normal erythrocyte AChE, one was in clinical remission and the other had active disease. Although the activity of this enzyme has been reported to be reduced in some disorders, in none has both frequency and degree of impairment approached that found in PNH.

Despite a relatively high concentration of AChE in red blood cells in human beings, the function of this erythrocyte enzyme remains unknown. Evidence [7] that AChE may be involved in the permeability of many different types of cells has been reviewed. Attempts have been made to incriminate AChE in the maintenance of normal permeability of certain mammalian erythrocytes. However, potassium transport has been demonstrated to be normal in the AChE-deficient PNH erythrocyte.[7c] In contrast, transport of radioactive phosphorus, phosphate turnover and ATP stability are abnormal.[8]

The AChE defect is present in young as well as old PNH erythrocytes. The enzyme activity is not further depressed during episodes of hemoglobinuria. Since only a small percentage of the PNH cells may be "sensitive" to hemolysis at any given time, present methods may be inadequate to assess a critical fall in enzyme activity in a small proportion of the total red cell population.

There is no clinical or serologic evidence that PNH is a heritable disorder.[4] Limited studies have revealed normal erythrocyte AChE activity in family members. No decrease in activity of those enzymes of the glycolytic scheme which have been studied[9] has been found in the PNH erythrocyte.

Initially the demonstration of decreased erythrocyte AChE activity in PNH seemed to provide an explanation for the sensitivity to lowered pH. Previous work[10] had shown that physostigmine inhibition of the AChE of normal mammalian red blood cells suspended in isotonic choline ester solutions rendered the cells more sensitive to hemolysis as the pH decreased. Furthermore, erythrocytes from those mammalian species with relatively less AChE activity hemolyzed more readily when the pH was lowered. Such observations were consonant with the "enzymic buffer system" hypothesis that AChE was the agent which protected the erythrocyte from the deleterious effects of low pH. When these experiments were repeated with use of AChE-deficient PNH cells instead of physostigmine-treated cells, the former did not show increased sensitivity to reduced pH (i. e., in solutions of isotonic choline esters).[11]

Despite the sensitivity to acidified serum, the PNH erythrocyte has a normal iso-electric point[4] and a normal capacity to buffer acidified serum.[7a] Such findings are not surprising since the buffering capacity of erythrocytes resides chiefly in the hemoglobin.

The nature of the PNH erythrocyte AChE abnormality has not been firmly established. Current evidence suggests an absolute deficiency rather than inhibition of AChE activity. Nevertheless, an inhibitor tightly bound to the enzyme has not been excluded.[7a] Still another possible explanation is that the enzyme is present in normal concentration but is structurally abnormal.

The current interest in organophosphorus inhibitors of cholinesterase (e. g., war gases) calls attention to another profitable application of the study of the PNH erythrocyte. Although the cells of the nervous system apparently bear the brunt of the deleterious effects of organophosphorus inhibitors of cholinesterase, nerve cells of human origin are not readily available for in vitro studies. The AChE-deficient PNH red blood cell might be an excellent tool for gaining information regarding the acetylcholine-cholinesterase system.

Despite the rather voluminous research on PNH, van den Bergh's classic observation that the PNH erythrocyte is peculiarly susceptible to hemolysis in acidified serum continues to defy explanation. Meaningful correlation of this observation with abnormalities in stromal morphology, "antibody receptors," phosphorus metabolism, lipid composition, and enzyme activity may yield a by-product rich in the knowledge of erythrocyte biochemistry.

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DISCIPLES OF DISSECTION

In the pristine days of recorded medical history the exiguous references to surgical anatomy in life or dissection in death lead one to a homely conclusion. The fabric of the human body was unknown. The lack of satisfactory anesthesia prohibited extensive surgery and the potential significance of dissection either was not appreciated by the physician, was feared for superstitious reasons, or was forbidden by Church and State. Failure to exploit dissection by at least one major civilization before the birth of Christ is somewhat surprising. Of all disciplines that are available to the contemporary medical scientist in his pursuit of the cause and treatment of disease, it was possible for only anatomy and gross pathology to have been developed 5,000 years ago. Attempts to identify an adequate practice of dissection or the study of anatomy in any of the pre-Hellenistic cultures of Asia, Asia Minor, Egypt, or Homeric Greece have been sterile. Presumably, dissection of man was considered unnecessary and animal dissection sufficient for the formal education of a physician. This is the preamble to a dissertation on dissection prepared by Kevorkian,[1] currently a resident in pathology at Pontiac General Hospital in Pontiac, Mich.

As time approached the Golden Age of Pericles, the quality of medical progress was not enhanced by interest in anatomy or pathology. The Greeks professed great respect for the human body and demanded rapid burial. It was believed that the deceased wandered furtively along the river Styx until the body was buried or cremated. Thus necessity permitted little time for dissection. There is no evidence that Hippocrates utilized dissection in his school of medicine. Human dissection did not become an accepted practice until the reign of Ptolemy of Macedonia, friend of Alexander the Great, in the third century B. C. Pliny describes Herophilos of Alexandria as the "first man to search into the causes of disease" through dissection. Rumors of the Alexandrian practice of human vivisection were used by later critics to detract from the glory of this medical era. Anatomic and pathological study was pursued sporadically in the Roman Empire, culminating in the contributions of Galen in the second century A. D. Galen established a system of general pathology and differentiated anatomy of position from anatomy of purpose, i. e., morphology from function. He had studied anatomy in Alexandria and never ceased to deplore that human dissection was no longer possible in Rome.

Undoubtedly, limited dissection was practiced during the Middle Ages, but descriptions are meager and the evidence is incomplete. Dissection came into its own once more after the fall of Constantinople and the establishment of the great universities of southern Europe. It has never relinquished its prime position since that time. Chairs of Anatomy were established, embalming was an accepted procedure, and eventually public sanction of dissection led to a decline of grave robbing by medical students and physicians. Scores of famous anatomists and pathologists may be documented in the 15th, 16th, and 17th centuries. These would include Leonardo da Vinci, Fallopius, Eustachius, Vesalius, Fernel, Harvey, Sylvius, and Malpighi.

Bichat laid the foundation for modern histology and histological pathology. This was accomplished without a microscope; instead he used chemicals and fine tools for meticulous dissection of about 600 human bodies at the Hôtel Dieu. "Dissect in anatomy, experiment in physiology, follow the disease and make the necropsy in medicine; this is a three-fold path, without which there can be no anatomist, no physiologist, no physician"; this was Bichat's philosophy. Matthew Baillie, nephew of John Hunter, prepared an Atlas of Pathology early in the 19th century. Rokitansky performed more than 30,000 autopsies at the Allgemeines Krankenhaus in Vienna between 1827 and 1866, and Virchow published his "Cellular Pathology" in 1858. He died in 1902. Thus, the 20th Century found itself the beneficiary of the arduous and fruitful heritage of many famous and perhaps even some forgotten masters of dissection.

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THE EXTRA CHROMOSOME IN MONGOLISM

Investigators[1] in Paris, France, reported last year the discovery of an extra chromosome in tissue cultures from several persons with mongolism. Soon thereafter, investigators[2] in Edinburgh, Scotland, examined the somatic chromosomes in six typical persons with mongolism and found that in all of them the diploid number of chromosomes was 47. This finding has been confirmed elsewhere, and it is now considered established that children with mongolism have 47 chromosomes. The normal number of chromosomes in human beings is 46.

The extra chromosome occurring in persons with mongolism is an acrocentric V-shaped chromosome in the smallest size range, with a heterochromatic region at one end closely resembling one of the normal autosomal pairs; it is thought to be an extra small autosome.

Few observations in recent years have created more stir and more theorizing, especially among geneticists and pediatricians. This does not, of course, imply that theories on the etiology of mongolism were not already abundant. At a conference in Cincinnati last October, sponsored by the National Association for Retarded Children, Dr. Josef Warkany,[3] professor of pediatrics at the University of Cincinnati and chairman of the conference, presented a list of 39 theories proposed in the past to explain the etiology of mongolism.

However, the impact of the discussion on the extra chromosome as it appears in Doctor Warkany's review of the conference indicated that the 39 theories of the past probably now will be replaced by "over 40 new theories." Many hypotheses, some long prevalent in the medical literature, appear now to be outdated, he said. The discovery of the extra chromosome in persons with mongolism, it would seem, will change the direction of etiological research and will stimulate, we hope, a new approach to a better understanding of this disease.

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ORGANIZATION SECTION

STATEMENT OF THE A. M. A. TO THE SUBCOMMITTEE ON HEALTH AND SAFETY, COMMITTEE ON INTERSTATE AND FOREIGN COMMERCE, HOUSE OF REPRESENTATIVES

H. R. 5260, FEDERAL HAZARDOUS SUBSTANCES LABELING ACT MARCH 14, 1960

Mr. Chairman and members of the Subcommittee:

I am Oscar Benwood Hunter Jr., of Washington, D. C., where I am engaged in the private practice of medicine as a pathologist. I am here today as a representative of the American Medical Association to endorse the principles of H. R. 5260, a bill to require the labeling of hazardous substances, and to make suggestions for its improvement. With me are Dr. Bernard E. Conley, Secretary of the Association's Committee on Toxicology, and Mr. Paul R. M. Donelan, the Association's Legislative Attorney.

Uniform legislation to require precautionary labeling of all chemical products containing hazardous substances has been an objective of medical and health groups for nearly a century. Over 75 years ago the American Medical Association adopted a resolution urging Congress and the various state legislatures to enact legislation to require lye to be sold as a poison and under a poison label. Later resolutions were adopted in 1910 and 1918 urging the proper labeling of caustic poisons. These actions culminated in the formation by the Association of a committee to obtain legislation regulating the sale of caustic products.

In 1923, the House of Delegates of the American Medical Association adopted a resolution which called attention to the fact that the domestic use of concentrated lye and other caustic alkalies and corrosive substances was a recurring cause of death and distressing disability among children. It recommended, in the interest of public health and safety, that the packaging, labeling and distribution of such substances be regulated by law. The Association's Committee thereafter prepared a model state law and a bill for introduction in Congress. The Federal Law was enacted in 1927, and the model state law has been enacted in a number of states.

Since that time many new compounds for household, commercial and industrial use have been introduced which are not covered by the above mentioned legislation. Presently, there is no broad law which requires the precautionary labeling of hazardous substances at the national level. Various attempts have been made in recent years to extend the scope of existing legislation to require precautionary labeling of potentially harmful chemicals in commerce. The first of these attempts was the Bingham bill of 1932 which called for the labeling of certain chemical products, particularly those involving injurious vapors. This bill served to focus attention on the need for a sustained, dynamic program for the development of precautionary labeling for hazardous chemicals.

Several years ago, at one of the periodic meetings of the American Medical Association's Committee on Toxicology with various chemical industry groups, a recommendation was made that the A. M. A. consider the development of model legislation to require precautionary labeling of household and industrial chemicals not so regulated. The Committee was subsequently authorized to undertake this task and has spent two years surveying existing legislation, reviewing various labeling schemes proposed in this country and abroad, and consulting numerous associations and qualified authorities. This study revealed the need for:

1. A broad and encompassing label law as a weapon in any successful attack on accidental poisoning from harmful chemicals. Lack of information about hazardous ingredients in cases of poisonings have enhanced their gravity by complicating or delaying treatment.

2. Directing such a law toward the reduction in careless handling and storage of potentially harmful products, which are found in and around the house, in small businesses, and in other areas where the control of exposure to chemicals is not as guarded as in the manufacturing process. The law should require informative labeling, which would include a list of hazardous ingredients, their potentialities for harm, directions for safe use, and first-aid instructions.

3. Label warnings based on the anticipated degree of danger and the use of words and symbols that facilitate recognition. In practice, however, few persons are sufficiently interested or informed to analyze the precise shades of meaning given to the signal words such as "danger," "warning" or "caution" and thereby act accordingly. Therefore consideration should also be given to the use of familiar warning symbols such as a flame for inflammable substances or a skull and crossbones for very poisonous substances because they are readily recognized and meaningful even to the illiterate.

The use of carefully chosen symbols in conjunction with the signal word "danger" for substances presenting the greatest hazard would facilitate recognition and bridge the language barrier.

4. Similar labeling standards for chemicals for export to foreign countries, thereby obviating the recurring complaint that less-than-standard products are sold to foreign purchasers.

As a result of the study, model legislation, quite similar in terms, objectives and method of approach to H. R. 5260 and S. 1283, its companion bill in the Senate, was drafted. The Association therefore endorses these bills in principle.

While we believe they are a step in the right direction, we believe that, to provide adequate protection for the use of such products in the home or at work, the legislation must be amended to (1) include package chemicals "for non-manufacturing purposes," (2) require use of warning symbols on containers of extremely dangerous substances, and (3) apply to hazardous substances being exported.

I would like to outline the Association's views on each of the above recommendations.

Section 2 (o) of H. R. 5260, which defines a "misbranded package," should be amended to apply to all hazardous substances "distributed as packaged chemicals for non-manufacturing purposes" rather than simply those "intended or suitable for household use."

The need for appropriate labeling of these products for household use has been amply demonstrated. I will therefore confine myself to the need for such protection for those engaged in non-manufacturing occupations.

By using the term "non-manufacturing," I mean those occupations where raw chemicals are not used as an ingredient of the product. Two-thirds of our 4.5 million business enterprises are either retail trade establishments, such as grocery stores, filling stations, restaurants, etc., or are service establishments, such as hotels, laundries and dry cleaners. These firms employ a major portion of the labor force and provide the least organized medium for maintaining the workers' safety.

Large chemical plants are among the safest places to work because of enforced safety rules. Plant safety directors continually emphasize the danger of poisoning and other hazards. In the chemical industry, a careless employee is an unprofitable one and, therefore, is liable to be discharged.

On the other hand, in a small business a careless employee is merely a potential accident statistic and is removed only through ignorance of the hazard and personal negligence. A janitor is not going to be fired when he uses an unlabeled cleaning solvent in an unventilated area. He may, however, suffer serious damage to his kidneys.

While the incidence of occupational injury attributable to chemical products is difficult to determine because only a few states keep records on the source of compensible work injuries, an indication of the extent of the problem can be obtained from the Occupational Disease Report published annually by the California Department of Public Health. These statistics are based on the "doctor's first report of work injury" derived from 80% of the working population that is subject to the California workmen's compensation act.

The California Occupational Disease Report for 1957 discloses 18,819 reports of injury. 39.8% of these injuries were attributable to chemicals. Over half (53%) of the injuries from chemicals occurred in manufacturing establishments which ranged from the making of confectionaries to the building of aircraft. Retail and service organizations accounted for 20% of such injuries and agricultural, construction, and governmental occupations, approximately 7%.

Dermatitis was the most common, accounting for 80% of the injuries. Systemic poisoning and lung injuries (chemical bronchitis and pneumonitis) accounted for 12% and 4%, respectively.

In terms of time loss from work, a fairly equal distribution prevailed among the three types of reactions.

While no information is available as to the number of injuries associated with unlabeled or poorly labeled chemical products, our concern is based on the belief that warning statements of the hazardous ingredients are needed just as much by workers who do not have the benefit of safety programs as they are in the home.

To limit the scope of new legislation to the phrase "suitable for household use" would be to maintain the same inherent weakness which brought criticism of the Federal Caustic Poisons Act. The restrictive scope and language of this statute is the basis for the dissatisfaction with it. To continue these restrictions under the guise of new and improved legislation is hardly a step forward and certainly will not meet the compelling need for better control of hazardous substances.

Section 2 (o) should also be amended to include appropriate safety warning symbols, such as the skull and crossbones, for various types of hazards associated with the more dangerous products.

In this connection, I should like to invite the Subcommittee's attention to the warning symbols adopted by the International Labor Organization and the United Nations. Simple and striking designs identify the following types of hazards: A skull and crossbones for poisons and dangerously toxic materials; a flame for inflammable substances; an exploding article for explosive substances; and a corroded hand for corrosive substances.

Consideration might be given to the use of background colors on warning labels to identify products which testing has shown can be used with reasonable safety, with some caution, or with great care because of dangerous ingredients. Green, yellow and red are commonly identified with safety, caution or danger and could be used as safety semaphores.

Surveys have shown that warning statements, as such, have little personal appeal. Apathy to printed warnings may be overcome with pictorial symbols and a safety semaphore utilizing familiar colors.

The proviso in Section 5 should be modified in such a manner as to require the same kind of labeling for packaged chemicals intended for export. In addition to protecting the ultimate consumer, such labeling is necessary to protect the American worker who may come in contact with the product in transit, the longshoreman who loads it on the boat and the seaman who transports it.

Section 5, as now written, would exempt such a product from the labeling requirements if it is labeled in accordance with the laws of the foreign country. It is our understanding that many countries do not have labeling laws. Even if the product is going to a country which has such laws, the American workers I have just mentioned would not be aware of the possible danger involved as a result of their inability to understand the foreign language. This problem could be mitigated by the use of the warning symbols and safety semaphores to which I have already alluded.

Finally, the use of similar labeling standards for packaged chemicals for export would obviate the recurring complaint that less-than-standard products are sold to foreign purchasers.

In closing, I would like to comment on a suggestion made to the Senate Committee with reference to the toxicological tests required by the bill. One industry spokesman advocated their omission in determining the necessity for the signal word "danger" and recommended that the term be applied only to very toxic substances which would also be labeled "poison." The reasons given for this proposed modification are that the present provisions would require "an enormous amount of laboratory work" and, in the words of a subsequent witness, "would tax laboratory facilities. . . ."

The American Medical Association does not believe that these recommendations are sound. Objection to toxicity standards, because they overtax testing facilities, is a recurring but unfounded fear. This fear has been expressed during the consideration of every legislative improvement in the regulation of chemicals from the Federal Caustic Poisons Act of 1927 to the current legislative debate over the regulations of chemical additives to foods. Admittedly, the provisions of H. R. 5260 would require more toxicity testing than has heretofore been undertaken for these products. However, improved protection for consumers against bodily injury necessitates and justifies the additional work. In addition, experience with older laws indicates that the economics of the problem will insure facilities and personnel to meet the demand. We strongly recommend maintaining the toxicity standards for "danger" set forth in H. R. 5260; furthermore, we recommend serious consideration be given to expanding the toxicity standards.

On behalf of the American Medical Association, I want to thank the Subcommittee for the opportunity to present its views on this legislation. If there are any questions, Dr. Conley, Mr. Donelan and I will be happy to try to answer them.

O. Benwood Hunter Jr., M.D.

STATEMENT OF THE A. M. A. TO THE SUBCOMMITTEE ON PROBLEMS OF THE AGED AND AGING, SENATE LABOR AND PUBLIC WELFARE COMMITTEE

April 4, 1960

Mr. Chairman and Members of the Subcommittee:

I am Dr. James Z. Appel of Lancaster, Pennsylvania, a member of the American Medical Association's Board of Trustees. With me today is Mr. C. Joseph Stetler, Director of the Association's Legal and Socio-Economic Division.

I should like to express the personal regrets of Dr. Louis M. Orr, the AMA's President, at his inability to appear today before this Subcommittee. He has asked me to explain that prior commitments made this impossible.

This Subcommittee has given representatives of the American Medical Association two previous opportunities to present its view on the medical care problems of the aged and aging. We appreciate it, just as we appreciate the invitation to appear again today.

Nonetheless, some of the material I expect to discuss has been covered in previous testimony and may therefore be familiar.

Let me begin, Mr. Chairman, by saying that all physicians, regardless of their type of practice, are able to observe at close hand the process of aging. Human beings age biologically as well as chronologically from the very moment of their birth. The doctor, in his day-to-day practice, therefore, becomes uniquely familiar with the process of aging—and with its attrition, its compensation, its inevitability, and its attendant problems.

No group is more intimately concerned with those problems than the members of the medical profession. Nor, in all probability, has any group devoted more study to the aging process or worked harder to find solutions to the many problems which accompany it.

First, you ask for information on the kinds and magnitude of health problems faced by older persons.

Let me begin with this statement: most older people are in good health. There are no such things as diseases of the aged. There are diseases among the aged, just as there are diseases to be found in any age group.

We hear a great deal about the prevalence of so-called "chronic illness" among older people. And so there is. But the term is generally misunderstood.

The term "chronic" simply refers to a recurrent condition, or one that persists over a period of time. It does not mean disability.

I, for example, am chronically ill. I have impaired hearing and use a hearing aid. But I am neither disabled nor incapacitated.

A diabetic is chronically ill but, with the help of insulin, can lead a perfectly normal life. Just a few years ago, a diabetic played on our Davis Cup Tennis team.

The chronically ill are simply impaired. Certain medical conditions limit certain of their capacities. They are not necessarily disabled.

This is why I make the point that most of our older people are in good health. They should not be thought of as debilitated and sick, for in the main they are not.

Dr. Ethel Shanas, of the University of Chicago, recently surveyed a representative group of older people with enlightening results. She found that 20 per cent or fewer of those over 65 were sick to the degree that illness limited their normal activity.

The consensus of those she interviewed seemed to be: "the way things are now, most people can expect to feel pretty good when they are 70."

I am not suggesting that the aged are as healthy as those in their prime, but I am saying that they are a great deal healthier than they are sometimes represented to be.

Our job as physicians is to keep the healthy in good health; and to help the sick regain their health to the greatest degree possible.

This is why medicine keeps stressing the positive aspect of health care.

We know, from long experience, that the best defense against sickness is full use by the individual of his physical, mental, and social capabilities.

And so the medical profession has been paying increased attention to the social, economic, and vocational factors which thwart the older person's use of his full capabilities and menace his good health.

Since our representative testified before this Subcommittee—last August—the Association and its constituent state medical societies have held eight regional conferences on aging.

Involved in these conferences were professional and lay people from all over the United States and from diverse fields of interest. And all learned from one another.

Briefly, here were some of our findings: 1. in over-all job performance, older workers are, in a majority of cases, as good as their younger counterparts. 2. they are generally more patient, persistent, and conscientious in doing their work. 3. in most instances they are more dependable, more loyal to the company, more safety conscious than younger workers; and they are less frequently absent from work. 4. half of those in large industries want to continue working past 65. And up to three-quarters of these employees were capable of continuing on their job in the opinion of their employers. 5. industrial employment counseling and flexible retirement programs have helped all concerned.

From the older persons themselves, we learned that most of them wanted to lead their own lives, and most of them are succeeding. They do not like to be thought of as members of a minority group, and they are just as independent in spirit as any other segment of our population—perhaps more so.

And finally, we learned that the bleak economic picture that has been painted of our older people is highly inaccurate. Income drops after retirement, yes. But needs are also more modest once the heavy expenses of raising a family are behind.

No other age group is likely to have as favorable a liquid asset position as the aged, three quarters of whom now own liquid assets in one form or another.

According to reports of the Social Security Bureau of Old Age and Survivors Insurance: "almost three of every four beneficiary couples owned their own homes—most of them free of mortgage—and the median equity in non-farm homes for the homeowners is $8,360."

It is important, in our opinion, to remember that the vast majority of our aged population is neither disabled by illness nor verging on bankruptcy. There are some who are, and the physicians of this country are determined to see that they get the best medical care available.

Let me make this point emphatically:

Medical care is available to every man, woman, and child in the United States regardless of his or her ability to pay for it. That care is not now denied, nor will it be denied.

Monsignor John O'Grady, who is Secretary of the National Conference of Catholic Charities, made this point effectively at one of our regional conferences. He warned that too many workers in the field of aging are, in effect, not seeing the forest for the trees. By concentrating on the small minority of our aged who represent an extreme situation—medically, emotionally, socially, or economically—they are winding up with a distorted picture.

They have magnified the problems of a minority segment to such an extent that their image of the total group has become blurred. They deduce, as a consequence, that most of our 15,000,000 older Americans are in poor health, are living on reduced incomes, are less able to contribute to their family or community, are no longer as capable of producing, and are living on the verge of an acute financial emergency.

The health problems of the aged, Mr. Chairman, can only be solved within the context of total health. They involve far more than hospitals or a doctor's care. They involve the older person's other requirements in life, whether these be housing, recreation, community understanding and acceptance, the right to be useful, the courtesy of being treated as individuals, or the opportunity of living as self-reliant, respected members of society.

But, if I were required to name the greatest problem faced by older persons today, I would state without hesitation that it is the problem of segregation–in employment, in the family, and in the community as a whole.

Until the people of this country abandon their misconceptions about aging, this segregation will continue. And, as long as our older people are thrust aside by a society which insists upon placing the accent on youth, a stream of lonely, idle, disheartened men and women will seek whatever emotional shelter they can find.

Too often, the only shelter available to them is the hospital, the nursing home, or the public institution.

Your second question concerns current methods of meeting health needs of older persons, including financing.

I will discuss this question in relation to the minority of older people who are ill and whose impairment restricts normal activities. We should keep in mind that the majority is in good health.

Viewing this aspect from the activities by the AMA state and community medical societies, we know that much has been accomplished in recent years. Our AMA Committee on Aging and similar committees established by all of the state medical societies have been extremely active. These committees are working at all levels to meet the health and medical care requirements of older persons. Aging and other committees of medical societies have conducted, and are in the process of conducting, such programs as: 1. Campaigns to correct deficiencies in state and local assistance programs for the needy. 2. Leadership in construction of additional facilities for care of the aged, such as nursing homes. The American Medical Association has cooperated with the American Nursing Home Association in conducting a study of nursing homes. The two Associations jointly developed and approved guides for medical standards in such facilities. These efforts toward higher standards have been simultaneous with continuing liaison with the American Hospital Association and the Public Health Service. 3. Promotion of health maintenance programs including specific campaigns to encourage periodic physical check-ups. 4. Stimulation of programs designed to permit the minority of older persons who are ill to remain in the beneficial environment of their homes. These programs include home-care, homemaker services, in-the-home rehabilitation and others which substantially reduce the cost of medical care. 5. Development of rehabilitative and restorative services to assist older persons toward fuller participation in life. 6. Creation of techniques to inform both patient and medical practitioner of the many medical and social services now available to the aged in their community. 7. Encouragement of the "progressive patient care" concept in hospitals. 8. Studies of the use of facilities by various age groups to develop more effective community priorities.

In connection with the last mentioned program, hospital studies tend to show that financing problems are more serious among younger than older patients.

Dr. Charles E. Staats, a Charleston, West Virginia surgeon, presented a documented example of this situation to your Subcommittee in Charleston on November 3, 1959.

Basing his submitted statement on records of the general hospital in Charleston which bears his family name, Dr. Staats said, "If unpaid hospital bills are a measure of financial insecurity of the aging group, our experience does not reflect the commonly held concept. 1.5% of our bills of the over-64 age group at this time are unpaid. In the over-85 age group 0.3% of the bills remain unpaid. In the over-85 group this amounts to $15 unpaid. In contrast, other patients under 65 had 14.9% of the hospital bills remaining unpaid. Our financial experience with elderly patients has been very satisfactory."

I am sure you have heard a number of times the statement that 60% of persons over 65 have incomes of under $1,000 annually. This may be true, but the statement is completely misleading. The fact is: Nearly 50% of the total population of our nation over the age of 14 has annual incomes under $1,000.

The Social Security Administration and the Federal Reserve Board have made studies which indicate that the median net worth of a retired worker with wife has increased in the short space of six years from $5,610 to $9,616. Twenty per cent of the aged have $5,000 or more net worth in savings accounts, checking accounts and savings bonds. Less than 10% of the entire population have net worth in this amount.

We are well aware that there has been a significant increase in the cost of health care in the last 50 years. In fact, the American Medical Association in February announced an initial grant of $100,000 to study health care costs in all their aspects, with resulting recommendations which we hope will produce efficiencies and financial savings. Comparing medical care of today with that available 50 years ago, however, is like comparing the wheelbarrow with a modern car.

Physicians themselves are doing what they can as individuals to soften medical expenses for persons over 65 with modest resources. Public welfare, religious and fraternal programs and donated services by doctors care for the indigent.

For the elderly with low family incomes, the AMA in December, 1958, called on state medical societies and physicians to expedite the development of low cost voluntary health insurance and prepayment programs. Physicians were asked to accept reduced compensation for their services which would make such development possible.

State medical societies and Blue Shield plans immediately responded to the AMA request. At the present, 39 plans in 36 states are offering nongroup coverage to persons over 65; 14 additional plans in 8 states are completing arrangements for such programs.

The health insurance industry is concurrently expanding coverage rapidly through special provisions for persons over 65. There is industry-wide emphasis on (a) continuation of insurance of older workers under group plans, (b) continuation of group insurance on retired workers and dependents, (c) conversions of group insurance to individual coverage at retirement, (d) individual policies purchased at advanced ages, and (e) insurance that becomes paid up at 65.

Your third question is related to the importance of preventive and rehabilitative services. These services are tremendously important. In fact, medicine's positive health program is based, in substantial measure, upon prevention. I refer to positive prevention as opposed to passive freedom from disease.

As I stated earlier, the great majority of older people are well. Actually, the word "well" can mean two things. It can mean health in its authentic sense, embodying the full use of all human capacities, with a consequent margin of safety against disease. Or it can mean a state of passive, medicated survival, which exists chiefly because of the manufactured absence of any physical or psychological ailment.

Clearly, positive health is fundamentally an individual responsibility, yet physicians play an important role by encouraging their patients to develop and follow health maintenance programs suited to their individual needs. This means, of course, that the physician serves as a health advisor as well as a healer. This is particularly true in encouraging older patients to live to their maximum capacity—to use their capabilities to the fullest.

This emphasis upon positive health extends also to the segment of our older citizens who are ill or disabled. It is the responsibility of all of us to recognize that our older citizens who are ill can benefit greatly from restorative programs. This means that we must put more and more emphasis upon helping the patient to help himself so that he can return as far as possible to independent living and to do this as soon as possible.

If a patient does not have the potential to return to active employment, too many people in the past, in my opinion, have been prone to write him off as incapable of rehabilitation. This is wrong. Moreover, it is unfair. Granted, there are sick older people for whom rehabilitation to full independence is not possible. But even with the most severely disabled patient—whether old or young—some degree of restoration can almost always be achieved.

Finally, Mr. Chairman, you ask for solutions to the problems of the aging.

We physicians would like nothing more than to help you define exactly what these problems are and then to offer a quick solution. I assume in asking this question that you are referring primarily to problems of financing the cost of health care.

Acknowledging that a problem of indefinite dimensions does exist, we believe it is one which will tend to diminish as time goes on. This is important, for there has been considerable pressure to create a permanent machinery for solving a temporary problem.

The growth of health insurance in this country has been little short of phenomenal in the past quarter century. Today, better than 127 million Americans are covered, and the amount of health insurance owned by aged people is growing at a rate faster than that of the population as a whole.

Private health insurance is available to the aged under a wide variety of plans, and at the moment some 43 per cent of those over 65 have some form of protection against the cost of health care.

According to the Health Insurance Association, 65 per cent of the aged, needing and wanting protection, will be insured by the end of this year; and this percentage will increase to 80 per cent by the end of 1965; and 90 per cent by 1970.

Furthermore, each year those who reach retirement age are better equipped financially to live self-sufficiently. For they are bringing with them, into their years of retirement, the protection of pension plans, which an ever-increasing number of employers are setting up. And, as most of them have carried health insurance during their working lives, they have learned to value its protection and continue it after retirement.

This becomes easier and easier to do under the many plans of health insurance now available—from policies paid up at 65 to continuation of coverage under a group plan.

In other words, I am saying that the problem of financing the health care of our older non-indigent people comes closer and closer to solution each day through private insurance and prepayment plans.

The solution to providing even better health care is being found by the efforts of private citizens, working together on a voluntary basis, at the community level.

Tremendous progress is now being made by these people. Retirement villages are being built. So are new nursing homes, and chronic disease centers. Home care programs are being expanded, recreational facilities are being set up, research programs are getting under way. And new approaches, such as progressive patient care, are being used in ever-increasing numbers.

The physician can and does provide health leadership within the community; the physician can and does work effectively to prevent ill health in his patients; the physician can and does treat and repair and cope with overt illnesses.

But, he cannot maintain the nation's health single-handed.

An older person can be hospitalized in a mental institution, for example, and in due course be discharged as cured. But if that person cannot find a job after returning to society, if he cannot receive the emotional support he needs, if he cannot win a place of acceptance within his family, his circle of friends, or his community, that person will be institutionalized once more.

As physicians, we try to keep our patients out of institutions and functioning in society. Our object is to help them lead lives as normal as possible.

We are after the same thing when we treat our older patients. We want to get them back into the main currents of everyday living. We want to get them back to independence and self-sufficiency as quickly, and as permanently, as possible. We do not want them—for the sake of their health—to believe that there is an emotional bonus in hospitalization or residence within the walls of an institution.

We are working, meanwhile, to give our older people access to the particular health facilities they may need. If they require hospital care, we want hospital beds to be available. And this applies to nursing home care, homemaker services, home care services, etc.

The rest is up to the realistic attitude with which friends, neighbors, families, employers, and communities contribute to the over-all effort that must be made.

It is our conviction, Mr. Chairman, that this contribution is increasing every year, and that the time is not far off when our aged will no longer be isolated from the rest of our society.

JAMES Z. APPEL, M.D.

THE SCIENTIFIC EXHIBIT AT WASHINGTON, D. C.

Application forms for space in the Scientific Exhibit at the Washington, D. C., Clinical Meeting of the American Medical Association, Nov. 28 to Dec. 1, are now available. They may be procured by writing directly to Dr. Charles H. Bramlitt, Director, Department of Scientific Assembly, American Medical Association, 535 N. Dearborn St., Chicago 10. Applications close on Aug. 1. The "Hull" award will be presented for the first time at this meeting to the best exhibit on a scientific subject which has not been previously shown at a medical meeting. The award will consist of a gold medal and an honorarium of $250. The winning exhibit will be approved for showing in the Scientific Exhibit at the 1961 annual meeting of the A. M. A. in New York City. Thomas G. Hull, Ph.D., will personally present the award to the recipient.

MOTOR ROUTES TO MIAMI BEACH

The convention-goer driving to Florida for the A.M.A. Annual Meeting in Miami Beach has the choice of a number of routes. From the entire Northeast and as far west as Cleveland and Detroit, the motorist usually chooses the turnpikes and freeways leading into the Washington-Baltimore area. From there, there are three choices: U. S. route 17, the oceanside route; U. S. route 301, the fastest and most direct (but be careful not to speed); and U. S. route 1, the old historic eastern route to the south, quite scenic and well supplied with top-notch accommodations.

From the area around Chicago and around the twin cities, St. Paul and Minneapolis, there are also many routes. The driver generally goes down through Vincennes, Nashville, Chattanooga, and Atlanta and into Jacksonville. There he may go south on U. S. route 1 and cut a little west to follow the Sunshine Toll Road.

Other midwestern routes follow the Mississippi River to Cairo, go south through western Tennessee into northeastern Mississippi, and then cut east to Montgomery, Alabama.

From the Pacific Northwest, the most direct route from Seattle is a diagonal down to Twin Falls, Idaho, along route 30, eastward along the same route number to Medicine Bow, where route 287 goes south into Denver and southeastward to a junction with one of the major transcontinental routes at Amarillo, Texas.

From San Francisco, the motorist heads southeast to U. S. route 66, which carries him to Amarillo. From there the route goes mostly eastward through Shreveport, La., around Jackson, Miss., and near Montgomery, Ala., where it makes a junction with a north-south route.

Motorists from Los Angeles usually follow a more southerly route which takes them near the Mexican border and the rim of the Gulf of Mexico and goes through El Paso, Houston, and Baton Rouge. From there, they can either visit or bypass New Orleans and go east on U. S. route 90. This route, like many others from the west and midwest, brings them into Tallahassee and the central lake section of Florida. The journey takes them through the orange groves areas.

The American Automobile Association advises persons whose time is limited to take a plane and rent a car when they get there. If they can spare the time to drive they can make sidetrips to many points of interest along the way.

Detailed routings and new tour books published by the American Automobile Association describing trips for its members are available through local motor clubs.

MEDICAL NEWS

ARIZONA

Plan Institute for Research and Training.—Ground will be broken late this summer at St. Joseph's Hospital, Phoenix, for a multi-million dollar research, treatment, and training institute to be known as the Barrow Neurological Institute. The center will emphasize research involving a score of diseases afflicting more than 16 million Americans. Construction of a $2,376,000 five-story wing was approved when Charles A. Barrow, Litchfield Park philanthropist, and his two children, Timothy and Cinda, announced an additional $500,000 gift in memory of his wife, Julia, who died last December. Mr. Barrow's latest donation brings to $1,120,000 the total made by his family. The institute is a memorial to his father, the late William E. Barrow, of Pennsylvania, who had close financial ties with Arizona. Reportedly the first neurological headquarters of its scope to be founded west of Montreal, the institute will be the third largest privately endowed center, treating both public and private patients, in the U. S. Its programs will be guided by a nonprofit, interdenominational group, recently incorporated, called the Neurological Sciences Foundation. The institute's activities will be divided into five major divisions: neurology, neurosurgery, neuropathology, neuroradiology, and experimental neurology. Dr. James W. Kernohan, currently president of the American Board of Pathology and professor of pathology at the Mayo Clinic, will become neuropathology division chairman when the institute opens its doors next year. In addition to an initial 50 beds for patient treatment, the center will house laboratories, surgeries, library, offices, and research facilities.

CALIFORNIA

New County Department of Mental Health.—With the approval of the Los Angeles County Medical Association, the board of supervisors of that county established a new department of mental health to coordinate and further develop community mental health services in Los Angeles County established under California's Short-Doyle Act. These services include voluntary inpatient, outpatient, and rehabilitation facilities, mental health education and information for the general public and for professional groups, and mental health consultation to community agencies. The director of this department is Dr. Harry R. Brickman, formerly in charge of the Psychiatric Clinic at the University of California Medical Center in Los Angeles.

Sir MacFarlane Burnet to Give Herzstein Lectures.—The 17th course of Morris Herzstein Medical Lectures will be delivered by Sir MacFarlane Burnet, M.D., director, Walter and Eliza Hall Institute of Medical Research, Melbourne, Australia, May 24, 26, and 27 at 8:15 p. m. in the Auditorium of the San Francisco County Medical Society, 250 Masonic Ave., San Francisco. The Herzstein Lectures were established in 1929 by the late Dr. Morris Herzstein, of San Francisco, to be given under the direction of Stanford University School of Medicine and the University of California School of Medicine. Sir MacFarlane will give three lectures on the subject, "Problems of Immunity," as follows:

May 24—Clonal Selection Theory After Three Years.
May 26—The Simonsen Phenomenon as a Laboratory Model of Autoimmune Disease.
May 27—Autoimmune Disease in Man—Some Theoretical Considerations.

Members of the medical profession and other interested persons are invited.

Dr. Meyer Honored.—Karl F. Meyer, Ph.D., San Francisco, was named the recipient of the 1960 Howard Taylor Ricketts Memorial Award of the University of Chicago. Dr. Lowell T. Coggeshall, vice-president in charge of medical affairs of the University of Chicago, announced the award. Dr. Meyer is director emeritus of the George Williams Hooper Foundation for Medical Research of the University of California and professor emeritus of experimental pathology, University of California. Dr. Meyer will visit the University of Chicago on June 6 to accept the award and to deliver the annual Ricketts Lecture, "Plague in the Light of Newer Knowledge," at 5 p. m. in Room P117, Billings Hospital. The recipient of the Howard Taylor Ricketts Memorial Award is traditionally announced on May 3, the anniversary of the death in 1910 of Dr. Ricketts, University of Chicago bacteriologist. Dr. Ricketts showed that ticks transmit Rocky Mountain fever. Dr. Meyer has been a member of the faculty of the University of California since 1913.

COLORADO

Institute on Alcoholism.—The Colorado Institute on Alcoholism will be held June 26-29 on the University of Colorado campus, Boulder. Dr. Marvin A.

Physicians are invited to send to this department items of news of general interest, for example, those relating to society activities, new hospitals, education, and public health. Programs should be received at least three weeks before the date of meeting.

Block, of Buffalo, N. Y., Chairman, American Medical Association Committee on Alcoholism, and Mrs. Marty Mann, executive director, National Council on Alcoholism, will give the principal addresses. It will be Colorado's first training program for professional workers in the personal and social problems of alcoholism. Co-sponsors are the Colorado Commission on Alcoholism and the University of Colorado's Extension Division and School of Nursing. Sessions will be open to nurses, social workers, rehabilitation personnel, educators, clergymen, probation and parole officers, correctional workers, personnel directors, police officers, and community leaders. Group meetings will be organized in professional clinics and in planned cross-sections of professional and community workers for case study. Dr. Edward J. Delehanty, chairman of the Colorado Commission on Alcoholism, will present "The Therapeutic Value of the Twelve Steps of Alcoholics Anonymous." Institute brochures are available from the Bureau of Continuation Education, 352 Chemistry Bldg., University of Colorado. Boulder, Colo.

CONNECTICUT

Hospital Opens Research Laboratories.—Hartford Hospital in Hartford recently opened three new floors of experimental research laboratories in the East Building. These facilities are to be used for fundamental research carried on by different services of the hospital. They consist of 10 fully equipped laboratories for chemical and biological investigation with auxiliary rooms. The large animal quarters have been refurbished and aerated with forced air. The laboratories were built with funds furnished partially by the Ford Foundation and by the National Institutes of Health.

Field Trials for Oral Poliomyelitis Vaccine.—The Poliomyelitis Study Unit at Yale University, New Haven, reported that 357 children, all under the age of 6 and living in five different areas of New Haven, are participating in the special field trial of the Sabin attenuated live poliovirus vaccine. The report was made as the project scheduled to run four months passed the halfway mark. Main purpose of the immunization program is to determine the effectiveness of the new vaccine in children under 6, for this is the age group which suffered most during the poliomyelitis epidemic in New Haven last summer. The Poliomyelitis Study Unit represents a team of doctors working under the direction of Dr. John R. Paul Jr., professor of preventive medicine, Yale School of Medicine. Participant members of the staff of the Yale Medical School and the New Haven City Department of Health include Drs. Robert H. Green, Dorothy M. Horstmann, Mary O. G. McCrea, and James C. W. Niederman. The New Haven field trial has been designed to yield information about optimum dosages as well as schedules of administration of the Sabin attenuated polioviruses when used as a vaccine. The participating children have been divided into three different groups and are receiving different dosages under different schedules. The project is being carried out with the cooperation of the New Haven City Health Department under the direction of Dr. Clement F. Batelli, director of public health, and the cooperation and active participation of the New Haven Visiting Nurse Association. It is supported by a grant from the National Foundation.

DISTRICT OF COLUMBIA

High School Students Win Research Scholarships.—Twenty District area high school juniors, 15 boys and 5 girls were awarded summer research scholarships at the Georgetown University Medical Center April 23. They were picked from 325 applicants, all with the "highest qualifications and recommendations." They will participate during July and August as members of actual research teams, working on funded research projects in basic or clinical science. The work planned for them was praised by Dr. Louis M. Orr, President, American Medical Association, and Surgeon General Leroy E. Burney, U. S. Public Health Service, as being in the interest of students and the medical and dental professions.

ILLINOIS

Annual Meeting of Anesthesiologists.—The Illinois Society of Anesthesiologists will hold its annual meeting May 23 at the Sheraton Hotel, Chicago, with a postgraduate anesthesia seminar to be held the following day. Participants at the meeting will include Drs. E. M. Papper, New York City; Frederick Van Bergan, Minneapolis; and John M. Brown, Atlanta, Ga. The seminar, acceptable for six hours credit in category II by the American Academy of General Practice, will include the following subjects:

Spinal Anesthesia.
Pediatric Anesthesia.
Obstetrical Anesthesia.
Muscle Relaxants.
Gaseous Anesthetic Agents.
Volatile Anesthetic Agents.
Intravenous Anesthetic Agents.
Local Anesthetics and Blocks.

For information, write Dr. Forrest J. Woodman, 9317 N. Harding, Evanston, Ill., Secretary.

Meeting of Surgeons.—The Illinois Surgical Society, Inc., will hold its annual clinical and scientific meeting Monday, May 23. Surgical clinics will be held at the Cook County Hospital, beginning at 8 a. m., with Dr. Karl A. Meyer serving as chairman of the surgical symposium. At the scientific meeting starting at 8 p. m., Dr. George T. Pack, New York City, associate clinical professor of surgery, Cornell University Medical College, will present "Clinical Aspect of Carcinoma Susceptibility and Carcinoma Immunity." Members of the medical profession are invited to all sessions. Discussions will follow each presentation. Information may be obtained from Dr. William M. McMillan, 122 S. Michigan Ave., Chicago 3, Secretary.

Chicago

Dustfall in Chicago.—Average total dustfall for Chicago during the month of March was 58.2 tons per square mile, a 5% increase over February of this year, according to research engineer Samuel Radner, Armour Research Foundation, Illinois Institute of Technology. Although the March dustfall was slightly higher than in February, it was 25% less than the dustfall for March, 1959 (77.8 tons). Highest reading in March was in the Loop: 169.4 tons. Another high reading was made at a recording station on the South Side: 93.4 tons. Lowest dustfall readings were made at a far Northwest Side station: 18.5 tons, and at a second South Side station: 29.2 tons per square mile.

MAINE

Personal.—Dr. Clyde I. Swett, Island Falls, was elected president of the New England Society of Obstetrics and Gynecology for 1959-1960. Also recently announced by the Pan-American Medical Association in Chicago is that Dr. Swett has been elected a member of their council.——Dr. Peter W. Bowman, superintendent, Pineland Hospital and Training Center, Pownal, has been appointed as consultant of the American Psychiatric Association for a mental health survey of the Province of British Columbia, Canada.

MASSACHUSETTS

Dr. Schmidt Named Department Head.—Dr. William Morris Schmidt's appointment as professor and head of the department of maternal and child health in the faculty of the Harvard School of Public Health was announced by Dr. John C. Snyder, dean of the faculty. His appointment will be effective on July 1. Dr. Schmidt will succeed Dr. Martha May Eliot, who will retire in July to become professor of maternal and child health, emerita. With the exception of a period when he served as medical advisor to the American Joint Distribution Committee, Dr. Schmidt has been a member of the faculty of public health at Harvard since 1949.

MICHIGAN

Fellowship in Public Health.—A graduate fellowship in public health is being offered by the Michigan Tuberculosis Association. The Werle–Bennett Graduate Fellowship is open to anyone with a bachelor's degree from a recognized college or university. Applicants must be qualified for admission to the University of Michigan School of Public Health but may study at any public health school. The basic fellowship is for $3,500 plus $500 for each dependent up to the maximum of $5,000 for one year. Applications for the grant should be made by June 1. Additional information and application blanks may be gotten from the Michigan Tuberculosis Association, 403 Seymour Avenue, Lansing. Recipients of the fellowship will be expected to work in Michigan for a voluntary tuberculosis association or in other public health areas for two years following graduation. The fellowship was named in honor of Theodore J. Werle, executive secretary of the Michigan Tuberculosis Association for 35 years, and Harry D. Bennett, who has served since 1922 as treasurer of the association. Christmas Seal contributions finance the Werle–Bennett fellowship.

MINNESOTA

Dr. Walters Elected to German Surgical Group.—Dr. Waltman Walters, senior surgeon of the Mayo Clinic and professor of surgery in the Mayo Foundation, Graduate School, University of Minnesota, was elected a corresponding member of the German Surgical Society at a recent meeting of the organization in Munich, according to information received from Dr. Willi Felix, of Berlin, president of the society. Dr. Walters, chief editor of the *Archives of Surgery,* has been active in encouraging the publishing of papers by German medical and surgical authors in American medical journals, and in asking American authors to publish papers in German medical and surgical journals, "as a means of improving medical and scientific relations between the two countries."

NEW YORK

Plan Unit for Narcotics Research.—A $300,000 grant has been made to the New York State Department of Mental Hygiene for construction of a narcotics research facility by the Division of Research Grants of the National Institutes of Health, according to Dr. Paul H. Hoch, State Commissioner of Mental Hygiene. The grant, matched by a similar appropriation of state funds, will go toward remodeling a wing of an existing building at Manhattan State Hospital, Ward's Island, N. Y., into a basic science laboratory devoted to research in drug biochemistry and physiology and in general neurochemistry. The laboratory will be part of the state's first full-time narcotics research unit. The new facility will include 20 laboratories, animal rooms, a library, conference room, and office space. A 55-bed narcotics center was established in another wing of the same building in September, 1959. This serves as the clinical unit of the narcotics research center which has both inpatient and outpatient facilities.

Society News.—At the annual meeting of the New York Rheumatism Association the following officers were elected: president, Dr. Ronald W. Lamont-Havers; vice-president, Dr. Sidney S. Berkowitz; and secretary-treasurer, Dr. Albert W. Grokoest. ——The New York Roentgen Society appointed the following officers for the year June, 1960, through May, 1961: president, Dr. Frank J. Borrelli; vice-president, Dr. William B. Seaman; secretary, Dr. Albert A. Dunn Jr., treasurer, Dr. Bernard S. Wolf; historian, Dr. Ramsay Spillman; and member of executive committee, Dr. Harold G. Jacobson.—— At a meeting Jan. 25, the following officers of the Rochester Roentgen Ray Society were elected: president, Dr. Charles E. Sherwood; vice-president, Dr. Theodore F. Van Zandt; and secretary-treasurer, Dr. Robert H. Greenlaw. The society meets on the last Monday of each month, September through May.

Report Increase in Rabies.—The number of cases of animal rabies in New York State continued to rise during the first three months of the year, Dr. Herman E. Hilleboe, State Health Commissioner, reported. As of March 31, 97 rabid animals were reported, compared with 26 for the same period in 1959. The disease has been most prevalent in the following counties: Allegany, 22; Steuben, 21; Erie, 15; Ontario, 12; and Cattaraugus, 9. During 1959, 475 laboratory confirmed cases of rabies in animals were reported, compared with 261 in 1958. Dr. Hilleboe said that in recent years the reported incidence of rabies has been cyclic in nature with peaks of decreasing magnitude occurring every three or four years, starting with the peak incidence of 1,155 cases reported in 1946. The pattern of heavy infection in Western New York, and lighter sporadic infection in the Eastern section, has again developed this year. Cases reported during the first three months of the year include foxes, 62; cows, 13; cats, 10; dogs, 4; skunks, 4; raccoons, 2; and horses and goats, one each.

New York City

Foreign Lecturer.—Dr. Arthur M. Sutherland, David Elder Infirmary, Glasgow, Scotland, presented "Cardiac Disease Associated with Pregnancy" April 26 at the Section on Obstetrics and Gynecology, New York Academy of Medicine. Dr. Alvin J. B. Tillman, Columbia-Presbyterian Medical Center, and Dr. Robert C. Knapp, New York Hospital-Cornell Medical Center led the discussion which followed.

Dr. Opie Receives Gold-Headed Cane.—The gold-headed cane of the American Association of Pathologists and Bacteriologists was conferred April 28 on Dr. Eugene L. Opie, who, although officially retired in 1941, works almost daily on research on liver cancers at the Rockefeller Institute for Medical Research. The honor, in the tradition of the gold-headed cane of the Royal College of Physicians in London, is awarded periodically to the physician who to the association "represents the highest ideals in pathology and medicine." Dr. Opie, the ninth pathologist to receive the cane in the association's 41-year history, was the first to observe that injury to the cells of the islands of Langerhans causes diabetes.

Personal.—Dr. J. Burns Amberson was honored by the American College of Physicians at its convocation in San Francico April 16, when he was named a master of the college. With Dr. Amberson's election, the number of living masters of the college was brought to 31. A past-president of the National Tuberculosis Association, Dr. Amberson has been general director of the New York Tuberculosis and Health Association since 1955.—— Dr. Charles D. May, editor of *Pediatrics*, was the guest speaker at the Alpha Omega Alpha initiation banquet of the University of Kansas School of Medicine April 27 in Kansas City. Dr. May delivered the annual William Root Memorial Lecture to staff and students on the campus, April 28. His subject was "Drugs and Doctors."

NORTH CAROLINA

Dr. Kinney Appointed Pathology Chairman.—Dr. Thomas D. Kinney was named professor and chairman of the pathology department at the Duke University Medical Center, Marcus E. Hobbs, Ph.D., dean of the university, announced April 25. The appointment is effective Sept. 1. Dr. Kinney is currently a professor of pathology at the Western Reserve University Medical School, Cleveland, and director of pathology at Cleveland Metropolitan General Hospital. He will succeed Dr. Wiley D. Forbus to the pathology department chairmanship. Dr. Forbus will continue to serve on the Medical Center faculty as a professor of pathology until his retirement in 1963. Dr. Kinney is chairman of the Pathology Study Section of the U. S. Public Health Service. He has served as a council member of the International Academy of Pathology and of the Society for Experimental Biology and Medicine; and as chairman of the general research committee of the American Society of Clinical Pathologists. Dr. Kinney is editor of *Laboratory Investigation*.

Organize Group of Blood Banks.—Some 50 persons representing 20 North Carolina blood banks met at the University of North Carolina School of Medicine and formed the North Carolina Association of

Blood Banks. The objective of the new organization is "the improvement of blood banks throughout the state and the better utilization of blood." An interim board of directors for the new association includes Dr. Bob Andrews, of Southeastern General Hospital, Lumberton, as president. The purposes of the association, as outlined in the articles of incorporation, are (a) to expand blood bank facilities to meet the needs for blood and its derivatives for every person in the state; (b) to promote and foster the exchange of ideas and materials and information relating to blood banking and transfusion services; (c) to foster and develop a clearing house or organization for the exchange of blood and/or blood credits within and without this state; and (d) to assist in the provision for, equipment for, and operation of blood banks. Plans are underway for a meeting in the fall in conjunction with technical workshop on blood banking methods. For information, write Dr. Robert Langdell, North Carolina Hospital, Chapel Hill, N. C., Secretary.

TENNESSEE

State Medical Election.—The following new officers of the Tennessee State Medical Association will serve until the next annual meeting, April 9-12, 1961: president, Dr. Ralph O. Rychener, Memphis; president-elect, Dr. William O. Vaughan, Nashville; speaker of house of delegates, Dr. Joseph W. Johnson Jr., Chattanooga; secretary-editor, Dr. R. H. Kampmeier, Nashville; vice-presidents, Drs. William T. Proffitt, Cleveland; J. Kelley Avery, Union City, and C. B. Roberts, Sparta; and executive director, Mr. J. E. Ballentine, 112 Louise Ave., Nashville, Tenn.

Dr. Woodruff to Go to Beirut.—Dr. Calvin W. Woodruff, professor of pediatrics, Vanderbilt University School of Medicine, Nashville, is resigning to accept appointment as professor of pediatrics and chairman of the department at the American University of Beirut. Dr. Woodruff's resignation will become effective June 30, and he will assume his new duties on Aug. 1. The American University of Beruit, sponsored by Americans since 1866, is the largest American institution outside the United States. It has an average of 2,500 students presenting 52 different nationalities and 21 religions. The Medical Division, founded 93 years ago, operates schools of medicine, nursing, pharmacology, and public health. The university also operates a teaching hospital of 230 beds with modern laboratories and research facilities.

Society News.—The Tennessee Radiological Society recently elected the following officers: president, 1960, Dr. George K. Henshall Jr., Chattanooga; president-elect, Dr. Ed H. Mabry, Memphis; vice-president, Dr. M. D. Ingram Jr., Nashville; secretary-treasurer, Dr. James J. Range, Johnson City. Councilors nominated for the American College of Radiology are Dr. Walter D. Hankins, Johnson City, and alternate, Dr. J. Marsh Frere, Chattanooga.—The Tennessee State Orthopaedic Society held its 12th annual meeting in Chattanooga, March 12. Dr. Robert G. Brashear was elected president; Dr. Paul E. Spray was elected vice-president; Dr. William F. Gallivan Jr. was elected secretary and treasurer. The 1961 meeting will be held in Knoxville.—The Memphis Thoracic Society, an organization of Memphis and Mid-South Thoracic surgeons, internists, and medical chest physicians, elected the following officers for 1960: Dr. Samuel Phillips, president, succeeding Dr. Francis H. Cole; Dr. Robert P. McBurney, vice-president; and Dr. William G. White, secretary-treasurer. Physicians in the Mid-South area are invited to attend the meetings.

TEXAS

Symposium on Space Flight.—"Psychophysiological Aspects of Space Flight," a symposium sponsored by the Southwest Research Institute, U. S. Air Force Aerospace Medical Center, will be held in San Antonio May 26-27. Maj. Gen. Otis O. Benson Jr., M. C., U. S. Air Force, commander, Aerospace Medical Center, Brooks Air Force Base, Texas, will open the program, which includes the following divisions: Technical Background and Experience, Clinical Problem Areas, and Problems of Human Reliability. The symposium, restricted in attendance to 400 persons, will bring together clinical and research scientists working in various psychophysiological disciplines. For information, write Mr. Jack Harmon, Symposium Coordinator, Southwest Research Institute, P. O. Box 2296, San Antonio 6, Texas.

GENERAL

Loans for Training in Obstetrics and Gynecology.—The American College of Obstetricians and Gynecologists has set up a Higher Education Loan Program (H-E-L-P) to enable resident physicians to complete their training in obstetrics and gynecology. Loans up to $5,000 will be made to help physicians through their specialty training period and early practice. H-E-L-P will start operations with an initial working fund of $36,000, contributed by the college and its district organizations. This will be added to through individual contributions and grants if necessary. For information, write to Mr. Donald F. Richardson, Executive Secretary, A.C.O.G., 79 W. Monroe St., Chicago 3.

Call for Papers on Poisoning.—The American Association of Poison Control Centers will hold its third annual meeting in the Wabash Parlor of the Palmer House, Chicago, on Tuesday, Oct. 18. A morning business meeting and an afternoon scientific session are planned. The meeting runs concurrently with the meeting of the Academy of Pediatrics, Oct. 17-20. There will be a discussion period after each paper. Any paper dealing with poisoning in general, and particularly as related to children, will be welcomed. It is requested that abstracts for each paper and the paper itself, be sent no later than Aug. 1 to Dr. Harry C. Shirkey, Chairman, Program Committee, American Association of Poison Control Centers, 712 S. 30th St., Birmingham, Ala.

Jurist Receives Psychiatrists' Award.—Judge David L. Bazelon, of the United States Court of Appeals in Washington, D. C., is the ninth winner of the American Psychiatric Association's $1,000 Isaac Ray Award. The award is given annually to a psychiatrist or member of the legal profession for furthering understanding between the two professions. As recipient, Judge Bazelon will deliver a series of lectures at the University of Chicago during the Academic School Year of 1960-1961, under the joint auspices of that university's law and medical schools. Judge Bazelon is known for his formulation of the Durham Decision which brought to American jurisprudence the concept that when criminal acts are perpetrated as the result of mental illness, the court will consider the nature of the illness of the accused.

Director Named for Heart Group.—Dr. Nathaniel H. Cooper was appointed associate medical director and director of community service and education of the American Heart Association. Dr. Cooper, formerly director of health of the Community Council of Greater New York, a position he has held since 1954, will be responsible for administering activities in the field of community service and education conducted nationally by the American Heart Association and by its affiliates and chapters throughout the country. These include programs of public education in cardiovascular disease, cardiac rehabilitation, school health services, cardiac clinics, and a variety of other services to aid heart patients and their families. Dr. Cooper is president of the National Conference for Health Council Work.

Decrease in Traffic Deaths in March.—The National Safety Council reported that the March traffic death toll was 16% below the same month last year—the greatest such decrease ever recorded for any month since early in 1947. The March figure of 2,400 deaths is contrasted with 2,860 deaths a year ago. The drop in March resulted in a January-February-March death toll this year 5% below the total for the same period in 1959. At the end of the first three months of last year the toll was running 5% above 1958. The traffic death totals for the three-month period were 7,680 this year against 8,080 in 1959. The traffic death toll recorded this March was the lowest for any March since 1949. The improvement was general across the country. Thirty-seven states showed decreases—the greatest number on record for any one month.

Poland Receives Health Units.—The New York *Times* reported that United States Ambassador Jacob D. Beam, presented four mobile health units to the Polish government March 31. The units, a gift from CARE, are fully equipped for mass inoculations of children against tuberculosis. Two are equipped with dental equipment and laboratories for work among underprivileged village children in Southern Poland. The four units represent a pilot project. CARE, the Cooperative for American Remittances to Everywhere, is planning to import other units to bring modern medication to Poland's backward areas. Since the resumption of its operations in Poland, CARE has brought about 8 million dollars worth of bulk foodstuffs, food packages, poliomyelitis vaccines, antibiotics, multivitamins, and specialized medical equipment to that country. This year's program will amount to 5 million dollars.

Grant for Hospital Design Research.—The U. S. Public Health Service has awarded the first grant ever given to a chapter of the American Institute of Architects, for hospital design research. The research project, which will cover a three-year study of the planning of hospital operating suites, will be directed by Mr. Robert Hyde Jacobs Jr., who plans to set up an office in New York City. The project was formulated by the Hospital and Health Committee, through its subcommittee on research. The project's work will include an investigation of routines carried on in operating suites, a survey of work being done in combatting hospital-acquired infections (insofar as this applies to the layout and equipment of operating suites), and an analysis of existing and projected operating suite plans, with the purpose of developing information to help hospital architects.

Meeting on Air Pollution Control.—The 53rd annual national meeting of the Air Pollution Control Association will be held May 22-26 at the Netherland-Hilton Hotel, Cincinnati. The program for the meeting, announced by Charles W. Gruber, chief, Cincinnati's Air Pollution and Heating Control Bureau, and conference chairman, will consist of an intensive review of all aspects of the Nation's air pollution problems. In all, 69 technical papers will be delivered in 18 sessions on specific air pollution problems. Among the subjects to be dealt with during technical sessions are community air pollution surveys, auto exhaust research, industrial air pollution control, agricultural research, and zoning, planning, and administration for air pollution control. One afternoon will be devoted to tours of industrial plants and research installations in the Cincinnati area doing "outstanding" work in air pollution control. Industrial exhibits also will be shown in an adjoining hall at the hotel. Social and ladies' programs are planned. Requests for registration information should be addressed to A.P.C.A. Annual Meeting, 2400 Beekman St., Cincinnati 14.

Meeting of Catholic Hospital Group.—The 45th annual convention of the Catholic Hospital Association of the United States and Canada will be held May 30-June 2 in Milwaukee. The Rev. John J. Flanagan, S.J., executive director of the association, announced that the convention theme will be "Improved Hospital Management Through Communication." Topics for the general sessions will include the keynote address, "The Importance of Communication," by Mr. Dan J. Forrestal, director of public relations, Monsanto Chemical Company, St. Louis, and the following subthemes:

Communication and the Communicator.
Type of Communication.
The Scope of Communication.
Overcoming Difficulties to Achieve the Objective.

Dr. William J. Lahey, director of medical education, St. Francis Hospital, Hartford, Conn., will serve as chairman at a sectional meeting, "Communication and the Medical Staff," June 1. For information, write the Catholic Hospital Association, 1438 S. Grand Blvd., St. Louis 4.

Annual Meeting of Gynecologists.—The 83rd annual meeting of the American Gynecological Society will be held May 30-June 1 at the Williamsburg Inn, Williamsburg, Va., and the medical profession is cordially invited. The following papers will include invited authors:

Autopsy Comparison of Cardiovascular Changes in the Castrate and Normal Woman, Dr. Edmund R. Novak and Tiffany J. Williams, Baltimore.
Polycystic Ovarian Disease—A Clinical and Experimental Study, Dr. Tommy N. Evans and Gardner M. Riley, Ph.D., Ann Arbor, Mich.
The Metabolism of Estrone-C^{14} Sulfate in Women, Dr. Gray H. Twombly and Mortimer Levitz, Ph.D., New York City.
Refractory Amenia in Pregnancy, Dr. Roy G. Holly, Omaha.
Blood Volume Changes in Pregnancy and the Puerperium. I. Does Sequestration of Red Blood Cells Accompany Parturition?, Drs. Jack A. Pritchard, Kenneth M. Wiggins, and John C. Dickey, Dallas, Texas.
Plasma Nonesterified Fatty Acids in Pregnancy. II. Experimental Modification, Dr. Richard L. Burt, Winston-Salem, N.C.

Dr. Karl H. Martzloff, Portland, Ore., will give the presidential address at noon, May 31. That evening, Dr. Owsei Temkin, director, Institute of the History of Medicine, Baltimore, will present an address following the annual dinner. For information, write Dr. Andrew A. Marchetti, Georgetown University Hospital, Washington 7, D. C., Secretary.

CANADA

Symposium on Extrapyramidal System and Neuroleptics.—The department of psychiatry of the University of Montreal is organizing an international symposium on "The Extrapyramidal System and Neuroleptics," to be held at the University of Montreal Nov. 17-19. This symposium will permit an exchange of ideas among those researchers interested in this subject from the point of view of anatomy, physiology, neurosurgery, and psychiatry. Admission to the symposium will be unrestricted, but participation will be by invitation only. Cooperating in the symposium are 10 Canadian provinces, the United States, and several European countries. There are two official languages, English and French, with simultaneous translation. For information, write Dr. Jean-Marc Bordeleau, Department of Psychiatry, University of Montreal, Montreal, Canada.

FOREIGN

Latin Proctology Group Not Related to Italian Gastroenterologists.—The board of directors of the Societa Italiana di Gastroenterologia, meeting in Bologna on March 6, was informed that an "International Symposium" on "Latin Proctology" was announced, to take place in Rome on May 13-14. The board wants to make it known that this symposium was not related in any way with the activities of the Societa Italiana di Gastroenterologia, which has its own Italian Section of Proctology.

Berlin Medical Faculty to Celebrate Anniversary.—The celebration of the 250th anniversary of the Humboldt-Universität zu Berlin Medizinische Fakultät (Charite) will be held in Berlin Nov. 6-19, in connection with the 150th anniversary of the Humboldt University. Applications for participation are to be directed to the Committee for the Preparation of the 250th Anniversary of the Charite, Berlin N 4, Schumannstrasse 20-21, ℅ Dozent Dr.med. habil. Dagobert Müller, Secretary of the Committee.

Histochemical Congress in Paris.—On Aug. 28-Sept. 3, the first International Congress of Histochemistry and Cytochemistry will be held in Paris, organized under the auspices of the Societe Francaise d'Histochimie in collaboration with other histochemical societies, in particular the American Histochemical Society, the Deutsche Arbeitsgemeinschaft fur Histochemie, the Societe Belge d'Histochimie, the Italian and Japanese histochemical societies, and several nonautonomous sections of histochemistry. Participants will include persons from Germany, France, U.S.A., Japan, Italy, Brazil, Belgium, Sweden, Denmark, England, and Switzerland. The provisional program is arranged under three sections: Physical Problems, Biochemical Data Applied to Histochemistry, and Applied Histochemistry. The registration fee is $25 for full membership, $20 for associate members. All correspondence on scientific Congress matters should be addressed to Dr. R. Wegmann, Secretary General, First International Congress of Histochemistry and Cytochemistry, Institut d'Histochimie Medicale, 45, rue des Saints-Peres, Paris, (6^e), France.

CORRECTION

Dr. Smiley and Medical Education Affiliations.—In a Medical News item on page 2089, April 30 issue of THE JOURNAL, erroneous information appeared concerning Dr. Dean F. Smiley, Evanston, Ill., and his present affiliations. Dr. Smiley left the Association of American Medical Colleges in 1957 to become full-time executive director of the Educational Council for Foreign Medical Graduates. He also left the editorship of the *Journal of Medical Education*. Dr. Richard H. Young, dean, Northwestern University Medical School, is secretary of A.A.M.C.; Dr. Ward Darley is its executive director. Dr. John Z. Bowers, dean, University of Wisconsin Medical School, is editor of the *Journal of Medical Education*.

CORRECTION OF AN INCORRECTION

In THE JOURNAL, March 12, page 1196, there appeared a manuscript modification of Dr. Benjamin W. Carey's letter entitled, "Photodynamic Response of a New Tetracycline." The correction which appeared in the April 30 issue was not the intended one. It should have read: "One word was added by the manuscript readers in the last sentence of the first paragraph of the first letter. The sentence should read, 'Extensive pharmacological and laboratory toxicity studies failed to demonstrate any significant difference from the other tetracyclines.' "

EXAMINATIONS AND LICENSURE

MEDICAL SPECIALTY BOARDS

AMERICAN BOARD OF ANESTHESIOLOGY: *Written.* Various locations, June 24. Final date for filing application was January 10. Sec., Dr. Forrest E. Leffingwell, 217 Farmington Ave., Hartford 5, Conn.

AMERICAN BOARD OF DERMATOLOGY: Final date for filing applications of candidates completing training by October 15, 1960 is March 1, 1961. *Written.* Several cities, June 5, 1961. *Oral.* Philadelphia, Oct. 13-16, 1961. Sec., Dr. Beatrice M. Kesten, One Haven Avenue, New York 32, New York.

AMERICAN BOARD OF INTERNAL MEDICINE: New York City, Nov. 14-17. Closing date for filing application is July 1. *Written.* Oct. 17. Closing date for filing application was May 1. Sec.-Treas., Dr. William A. Werrell, One West Main St., Madison 3, Wis.

AMERICAN BOARD OF NEUROLOGICAL SURGERY: Examination given twice annually, in the spring and fall. In order to be eligible a candidate must have his application filed at least six months before the examination time. *Oral.* New Haven, Nov. 6-9. Sec., Dr. Donald D. Matson, 300 Longwood Ave., Boston, Mass.

AMERICAN BOARD OF OBSTETRICS AND GYNECOLOGY: Applications for certification in Part I, new and reopened, and requests for reexamination in Part II are now being accepted. Deadline for receipt of applications is August 1, 1960. After July 1, 1962, a minimum of three years of approved progressive residency training will be required. Training by preceptorship will no longer be acceptable. The initiation of preceptorships will not be approved after July 1, 1960. Sec., Dr. Robert L. Faulkner, 2105 Adelbert Road, Cleveland 6.

AMERICAN BOARD OF OPHTHALMOLOGY: *Written.* Jan. 23, 1961. Deadline for filing applications is July 1. *Oral.* Chicago, Oct. 3-7. Sec., Dr. Merrill J. King, Box 236 Cape Cottage Branch, Portland, Maine.

AMERICAN BOARD OF ORTHOPAEDIC SURGERY: *Oral and Written, Part II.* Miami Beach, Jan. 3-5, 1961. Final date for filing application is July 1. Sec., Dr. Sam W. Banks, 116 South Michigan Ave., Chicago 3.

AMERICAN BOARD OF OTOLARYNGOLOGY: *Oral,* Chicago, Oct. 3-6. Final date for filing application was April 1. Sec., Dr. Dean M. Lierle, University Hospitals, Iowa City.

AMERICAN BOARD OF PEDIATRICS: *Written.* New York City, January 1961. Final date for filing application is Dec. 1. Administrative Sec., Mrs. Eleanor J. Mitchell, Rosemont, Pa.

AMERICAN BOARD OF PHYSICAL MEDICINE AND REHABILITATION: *Oral and Written.* New York, June 17-18. Sec., Dr. Earl C. Elkins, Mayo Clinic, Rochester, Minn.

AMERICAN BOARD OF PROCTOLOGY: *Oral and Written, Parts I and III,* Philadelphia, Sept. 24. Final date for filing application is June 30. Sec., Dr. Stuart T. Ross, 520 Franklin Ave., Garden City, N. Y.

AMERICAN BOARD OF PSYCHIATRY AND NEUROLOGY: New York, New York, Dec. 12-13, New Orleans, Mar. 20-21, 1961. Sec., David A. Boyd, Jr., 102-110 Second Ave., S.W., Rochester, Minn.

AMERICAN BOARD OF RADIOLOGY: *Examination.* Cincinnati, June 6-10; Dec. 10-13. Deadline for filing applications for the June examination was Jan. 1. Filing deadline for the December examination is July 1. A special examination in Nuclear Medicine (for those diplomates in Radiology or Therapeutic Radiology) will be offered provided there are sufficient applications. Sec., Dr. H. Dabney Kerr, Kahler Hotel Bldg., Rochester, Minn.

AMERICAN BOARD OF SURGERY: *Written.* (Part 1), Various Centers, Dec. 7. *Candidates are urged to apply several months before completion of training requirements.* The closing date for filing applications is August 1. Those completing training requirements after September 30 cannot be considered for the December Part I examination of the same year. *Oral.* (Part II)—New Haven, Sept. 26-27; Indianapolis, Oct. 24-25; Buffalo, Nov. 14-16; Nashville, Dec. 12-13; Philadelphia, Jan. 16-17; Houston, Feb. 13-14; Columbus, Ohio, Mar. 13-14; New York City, April 19-20; Portland, Ore., May 15-16; San Francisco, May 18-19. No examinations will be held in June, July or August. Sec.-Treas., Dr. John B. Flick, 1617 Pennsylvania Blvd., Philadelphia 3.

BOARD OF THORACIC SURGERY: *Written.* Various centers throughout the country, Sept. 9. Final date for filing application is July 1. *Oral.* Oct. 1960. Final date for filing application is July 1. Sec., Dr. Wm. M. Tuttle, 1151 Taylor Ave., Detroit 2.

AMERICAN BOARD OF UROLOGY: *Written.* December. *Oral-Clinical.* Chicago, February 1961. Exec. Sec., Mrs. Ruby L. Griggs, 30 Westwood Road, Minneapolis 26.

GOVERNMENT SERVICES

DEPARTMENT OF DEFENSE

Aerospace Medical Association Meeting.—Retirement point credits may be earned by reserve medical corps officers who attend the 31st annual meeting of the Aerospace Medical Association at the Americana Hotel, Miami Beach, Fla., May 9 to 11. This authorization covers eligible physicians who are reserve medical corps officers of the United States Army, Navy, or Air Force on inactive status. At this meeting more than 250 leading aerospace bioscientists will present reports of their research work.

ARMY

Aeromedical Symposium.—An Aeromedical Symposium will be held at the San Carlos Hotel, Pensacola, Fla., on June 7 to 9. Sponsored by the United States Army Board for Aviation Accident Research, the symposium is designed to orient staff surgeons and hospital commanders to areomedical factors in aircraft accidents. Vice-Admiral Robert Goldthwaite, U. S. N., chief of Naval Air Training at Pensacola Naval Air Station, is scheduled to welcome those attending the "Annapolis of the Air." Prominent speakers will include Dr. Neal S. Warren, aviation psychologist from the University of Southern California, whose subject will be "Psychological Problems in Modern Aviation"; Dr. Charles I. Barron, medical director of Lockheed Aircraft Corporation, whose subject will be "Medical Aspects of Aircraft Accidents Investigation"; Col. John P. Stapp, M. C., U. S. A. F., chief of the Aerospace Medical Laboratory at Wright Air Development Center, who will speak on "Human Tolerance to G Forces in Aircraft Accidents"; Capt. W. M. Wurzel, M. C., U. S. N., chief of the aeromedical division of the Naval Aviation Safety Center, whose subject will be "Naval Flight Surgeon Program: Contribution of Navy Flight Surgeons to Accident Prevention"; Lieut. Col. R. B. Austin, M. C., U. S. A., chief of the aviation branch of the office of the surgeon general, Department of the Army, whose subject will be "The Assignment and Utilization of Army Aviation Medical Officers"; and Col. Frank Townsend, M. C., U. S. A. F., director of the Armed Forces Institute of Pathology, whose subject will be "Importance of Pathology and Autopsy in Aviation Accidents."

NAVY

New Hospital.—Dedication ceremonies for the new U. S. Naval Hospital, Portsmouth, Va., were held on April 22. The new hospital, the tallest building in the Norfolk-Portsmouth complex, replaces the original naval hospital in Portsmouth, which was built between 1827 and 1832. The dedicatory address was given by Rear Adm. Edward C. Kenney, deputy and assistant chief of the bureau of medicine and surgery, and the new hospital was accepted by Rear Adm. H. J. Van Peenen, its commanding officer.

Retirements.—Capt. Leonard H. Barber, M. C., U. S. N., after more than 20 years of active naval service was retired on March 31. His last assignment was to the U. S. Naval Hospital, Oakland, Calif. ——Capt. Clinton K. Higgins, M. C., U. S. N., was retired after more than 19 years of active naval service. His last assignment was to the U. S. Nava Dispensary, Norfolk, Va.——Capt. Jerry T. Miser M. C., U. S. N., was retired after more than 32 year of active naval service. He was last assigned a the U. S. Naval Station, Seattle.

New Assignment.—Capt. John W. Albrittain, M. C. U. S. N., has taken over as director of the bureau of medicine and surgery's professional division, replacing Capt. Malcolm W. Arnold, M. C., U. S. N Captain Arnold assumed command of the U. S Naval *Medical School, Bethesda, Md.*, on March 18. *Before* Captain Albrittain's new assignment h was head of the bureau's training branch.

Captain Barr Honored.—A bureau of medicine an surgery certificate of exceptional service was presented to Capt. Normal L. Barr, M. C., U. S. N (ret.), during ceremonies in the office of Surgeo General B. W. Hogan in March. A former directo of the bureau of medicine and surgery's astronautical division, Captain Barr retired from the Nav last September after *more* than 21 years of activ service. The citation on the certificate states i part, "For his brilliant research which has enhance the readiness and competence of the naval service in Fleet Defense and its medical-aeronautical an astronautical operations."

VETERANS ADMINISTRATION

Mental Disease Program.—Veterans Administration mental hospitals are putting the families of patients on the hospital team. The Lexington, Ky., VA hospital uses a successful method carried through by the patients themselves. They call it "Family Acquaintance Day." With the active encouragement of hospital officials, the 74 patients of one ward invited their families to come to Lexington and spend a whole day with them, seeing at first hand the life they lead in the hospital. Each patient signed an individual letter prepared for his family. The results exceeded expectations; 150 visitors from 50 families came. One group traveled 800 miles for the occasion. Six states were represented. The patients were dressed up expectantly to greet their families.

A program of short welcoming talks by the hospital manager, the chaplain, and medical and nursing members of the staff greeted the visitors. Family groups were introduced to other families, and a photographer was on hand to snap informal family photographs. The visitors were shown samples of work done by patients in the hospital hobby shop and viewed motion pictures of a day's outing the patients had taken to a nearby state park. Light refreshments were served. One mother said, "I had no idea it was like this. I don't know what I expected, but I feel better about everything and I will come now more often." A patient said, "I really can't believe they're here. They kept saying they would come some time but I thought they wouldn't make it." Hospital officials were enthusiastic over the beneficial results. One said, "In this type of illness, the patient's family and friends are needed more than in any other kind."

PUBLIC HEALTH SERVICE

Nutritional Survey in Chile.—In response to a request from the government of Chile, a team of United States experts began on March 28 a 70-day survey of the nutritional status of the Chilean population. The purpose of the study is to assess the current standards and needs of the people, to formulate practical recommendations for improvement consistent with the country's resources, and to provide technical assistance for the development of standard ration requirements and local nutritional services.

The survey was arranged by the Interdepartmental Committee on Nutrition for National Defense, an agency of the United States which operates administratively through the National Institute of Arthritis and Metabolic Diseases, National Institutes of Health, Bethesda, Md. Team members include physicians, biochemists, food technologists, and others who will work side by side with Chilean personnel during the survey. Laboratory equipment and supplies, which have already been shipped to Santiago, will be turned over to the Chilean government under mutual assistance program procedures on completion of the survey.

United States members of the survey team are Dr. William F. Ashe Jr., head of the department of preventive medicine, Ohio State University, Columbus, Ohio, survey director (clinician); Dr. Carl A. Baumann, of the college of agriculture, department of biochemistry, University of Wisconsin, Madison, Wis., deputy survey director and laboratory director; Lieut. Col. Marion E. McDowell, M. C., of the U. S. Army Medical Research and Nutrition Laboratory, Fitzsimons Army Hospital, Denver, clinician; Dr. John H. Browe, director of the bureau of nutrition, State of New York Department of Health, Albany, N. Y., clinician; Dr. Elizabeth H. Voris, of Bethesda, Md., clinician; Mr. James H. Blanton, of the Medical College of Alabama, University of Alabama Medical Center, Birmingham, Ala., medical assistant; Dr. Ronald R. Johnson, of the animal science department, Ohio Agricultural Experiment Station, Wooster, Ohio, biochemist; Dr. Leonard W. Aurand, of the department of animal industry, School of Agriculture, North Carolina State College, Raleigh, N. C., biochemist; Dr. LeRoy Voris, executive secretary of the food and nutrition board of the National Research Council, Washington, D. C., nutrition officer; Dr. Paul L. Pavcek, of Milwaukee, nutrition officer; Dr. Clinton O. Chichester, of the College of Agriculture, University of California Agricultural Experiment Station, Davis, Calif., food technologist; Mr. Edwin B. Bridgforth, of the School of Medicine, Vanderbilt University, Nashville, Tenn., statistician; Dr. Carol J. Witkop Jr., of the National Institute of Dental Research, Bethesda, Md., dentist; Miss Joan M. Gaiser, of the National Institute of Dental Research, Bethesda, Md., laboratory technician; and Mr. William A. Drake, of the department of photography, Ohio State University, Columbus, Ohio, medical photographer.

Cerebral Palsy.—The medical research attack on cerebral palsy is described by the U. S. Public Health Service in a new brochure, "Cerebral Palsy—Hope Through Research," in which some known causes of the disorder are explained, the main types and extent of the condition are described, and helpful treatment is reviewed. The publication also tells of pioneering efforts to overcome this chronically disabling condition that affects more than 500,000 persons in the United States. The leaflet was prepared by the National Institute of Neurological Diseases and Blindness and is listed as Public Health Service Publication no. 713 and Health Information Series no. 95. Single free copies may be obtained from the Public Service, Washington, D. C. Quantity orders cost $3.00 per 100 copies from the Superintendent of Documents, U. S. Government Printing Office, Washington 25, D. C.

ARMED FORCES EPIDEMIOLOGICAL BOARD

New President.—Dr. Gustave J. Dammin, professor of pathology at Harvard Medical School, was elected president of the Armed Forces Epidemiological Board, replacing Dr. Thomas Francis, chairman of the department of epidemiology at the School of Public Health of the University of Michigan, who had served as president of the board since Jan. 1, 1958. Members of the AFEB are appointed by the Secretary of the Army, and the members elect their own president.

American Board of Dermatology; member of the American Academy of Dermatology and Syphilology; professor emeritus of dermatology and syphilology at the New York Polyclinic Medical School and Hospital; died March 18, aged 84.

Morris, Abraham Samuel Ⓜ Haverhill, Mass.; Boston University School of Medicine, 1914; for many years city physician; a staff member of the Hale Hospital; died March 14, aged 70, while vacationing at Miami Beach, Fla.

Mugrage, Ralph McClellan Ⓜ Captain, U. S. Navy, San Juan, P. R.; University of Cincinnati College of Medicine, 1932; veteran of World War II; senior medical officer at the U. S. Naval Station; fellow of the American College of Surgeons; died March 13, aged 55.

Murphy, Christopher Joseph Ⓜ Arlington, Va.; Georgetown University School of Medicine, Washington, D. C., 1915; for many years practiced in Washington, D. C., where he served as deputy district coroner, a member of the Board of Police and Fire Surgeons, on the faculty of his alma mater, and was associated with the Providence Hospital, where he served an internship; veteran of World War I; died in the Alexandria (Va.) Hospital March 23, aged 67, of congestive heart failure.

Nelson, Charles Frederick Ⓜ Cleveland; University of Wooster Medical Department, Cleveland, 1897; member of the American Academy of Ophthalmology and Otolaryngology; for many years a medical consultant for the New York Central, the Erie, the Baltimore and Ohio, and other railroads; died March 17, aged 84.

Newport, Pearce Everett, Clarinda, Iowa; State University of Iowa College of Medicine, Iowa City, 1924; veteran of World Wars I and II; died March 12, aged 64.

Nichols, William Madison, Niagara Falls, N. Y.; Hospital College of Medicine, Louisville, Ky., 1905; died in Buffalo March 6, aged 87.

Ochsner, Rudolph John, San Jose, Calif.; Western Reserve University Medical Department, Cleveland, 1908; served as chief of the subdivision of child hygiene in the Cleveland Department of Health; died in the San Jose Hospital March 16, aged 89, of carcinoma of the lung.

Olson, Carl Theodore, St. Petersburg, Fla.; Rush Medical College, Chicago, 1919; member of the Industrial Medical Association and for his work as head of its Workmen's Compensation Commission received the Workmen's Compensation Award for meritorious service; formerly medical director for the Fansteel Metallurgical Corporation in North Chicago; founder and emeritus member of the Medical Directors Club of Chicago; served on the editorial board of *Journal of Industrial Medicine and Surgery;* died April 1, aged 66, of coronary occlusion.

Pitchford, John Dalton Sr. Ⓜ Sylacauga, Ala.; Emory University School of Medicine, Atlanta, 1922; member of the American Academy of General Practice; resident physician at Drummond-Fraser Hospital; died in the University Hospital, Birmingham, March 8, aged 62.

Rainforth, Selden Irwin, Coral Gables, Fla.; Johns Hopkins University School of Medicine, Baltimore, 1903; formerly practiced in New York City; died March 7, aged 81.

Reichard-Esteves, William Ⓜ San Juan, P. R.; Universite de Lausanne Faculte de Medecine, Switzerland, 1938; specialist certified by the American Board of Otolaryngology; fellow of the American College of Surgeons; interned at the Presbyterian Hospital, where he was a member of the staff; associated with the Veterans Administration Center; assistant clinical professor of otolaryngology at the University of Puerto Rico School of Medicine; died in Guaynabo, Jan. 13, aged 48.

Sanderson, John W. Ⓜ Oreland, Pa.; Baltimore Medical College, 1906; formerly practiced in Baltimore; died in Chestnut Hill March 18, aged 81.

Savery, Charles Edward, Deerfield Beach, Fla.; Indiana University School of Medicine, Indianapolis, 1914; specialist certified by the American Board of Ophthalmology; member of the American Academy of Ophthalmology and Otolaryngology; formerly practiced in South Bend, Ind.; died Feb. 13, aged 71.

Schurman, Emil William, Yonkers, N. Y.; Bellevue Hospital Medical College, New York City, 1898; died March 11, aged 83.

Schwartze, Henry, Portland, Ore.; Tulane University School of Medicine, New Orleans, 1931; served on the staff of the Florida State Hospital in Chattahoochee, Fla.; died in the Veterans Administration Hospital Feb. 28, aged 60.

Seabrook, Dean Baynard Ⓜ Portland, Ore.; University of Oregon Medical School, Portland, 1923; specialist certified by the American Board of Surgery; fellow of the American College of Surgeons; veteran of World Wars I and II; clinical professor of surgery at his alma mater; past-president of the North Pacific Surgical Society and the University of Oregon Medical Alumni Association; died March 5, aged 62.

Sentell, Newton Washington, Decatur, Ga.; Tulane University School of Medicine, New Orleans, 1914; served in the regular Army; veteran of World War I; died March 12, aged 70.

Sheldon, Russell Firth Ⓜ Boston; Harvard Medical School, Boston, 1911; fellow of the American Society of Anesthesiologists, Inc.; past-president and for many years secretary of the Boston Society of Anesthesiologists; veteran of World War I; associated with the Massachusetts General Hospital, where he died March 11, aged 74.

Simpson, Reuben Spencer Ⓜ Lyons, N. Y.; Cornell University Medical College, New York City, 1909; veteran of World War I; associated with the Lyons Hospital, where he died March 4, aged 78.

Simpson, William Elihu, Rock Hill, S. C.; Medical College of South Carolina, Charleston, 1915; past-president of the South Carolina Pediatric Society, Alumni Association of the Medical College of South Carolina, the Fifth District Medical Society, the York County Medical Society, and the Rock Hill Medical Club; member of the American Academy of General Practice; died March 10, aged 76.

Sparks, John Edgar Ⓜ San Antonio, Texas; University of Tennessee College of Medicine, Memphis, 1910; author of "An M.D. the Hard Way"; died March 9, aged 82.

Spencer, Joseph Ray, South Mills, N. C.; Medical College of Virginia, Richmond, 1915; veteran of World War I; died in Albemarle March 11, aged 68.

Steele, S. Clark Ⓜ Brave, Pa.; Balitmore Medical College, 1902; died March 8, aged 82.

Stueart, John B., Norman, Ark.; University of Arkansas School of Medicine, Little Rock, 1903; died Feb. 29, aged 81.

Telser, Stanley Edward Ⓜ Chicago; University of Illinois College of Medicine, Chicago, 1937; veteran of World War II; specialist certified by the American Board of Internal Medicine; served on the faculty of his alma mater and the Chicago Medical School; medical director of the Chicago Health Center of the AFL-CIO International Ladies Garment Workers Union; associated with the Mount Sinai Hospital; killed March 17, aged 48, in the crash of an airliner near Tell City, Ind.

Trotter, James Patten Ⓜ Yonkers, N. Y.; Columbia University College of Physicians and Surgeons, New York City, 1907; veteran of World War I; served as surgeon of the fire department; died in the Yonkers General Hospital March 18, aged 78.

Van Wormer, Frank Burton Ⓜ Mechanicsburg, Ill.; Milwaukee Medical College, 1912; died Feb. 17, aged 71, of cholecystitis and acute cholelithiasis.

Wallen, LeRoy John Ⓜ Sault Ste. Marie, Mich.; Detroit College of Medicine and Surgery, 1933; interned at the Grace Hospital in Detroit and the Shurly Eye, Ear, Nose and Throat Hospital in Detroit; veteran of World War II; died in the Chippewa County War Memorial Hospital March 7, aged 56.

Watson, Robert William, Rapid River, Mich.; University of Michigan Medical School, Ann Arbor, 1918; served on the staff of the Highland Park (Mich.) General Hospital; died in the Mayo Clinic, Rochester, Minn., March 12, aged 66.

Wheelon, Charles Homer Ⓜ Seattle; St. Louis University School of Medicine, 1918; specialist certified by the American Board of Internal Medicine; fellow of the American College of Physicians; member of the Endocrine Society; on the staff of the Columbus Hospital; died March 12, aged 71.

Wiseman, Bruce Kenneth, Columbus, Ohio; born in South Bend, Ind., March 1, 1898; Indiana University School of Medicine, Indianapolis, 1928; specialist certified by the American Board of Internal Medicine; member of the Central Society for Clinical Research and the American Society for Experimental Pathology; fellow of the American College of Physicians; joined the faculty of the Ohio State University College of Medicine in 1930, serving first as assistant professor of medical research, in 1936 named associate professor, in 1939 professor, and in 1945 appointed chairman of the department of medicine; at one time assistant in the department of bacteriology and pathology at the Rockefeller Institute for Medical Research in New York City; served as associate editor of the text book "The Practice of Medicine" and associate editor of the *Archives of Internal Medicine;* associated with the University Hospital, where he died March 15, aged 62, of cerebral hemorrhage.

Woodbridge, Jahleel Hamner, Pueblo, Colo.; Washington University School of Medicine, St. Louis, 1904; past-president of the Pueblo Pathological Society; veteran of World War I; associated with the Parkview Episcopal and St. Mary-Corwin hospitals, died March 6, aged 81, of acute myocardial infarction.

Zimmermann, Harry Bernard, St. Paul; born in St. Paul in 1885; Columbia University College of Physicians and Surgeons, New York City, 1909; member of the founders group of the American Board of Surgery; member of the American Surgical Association, Western Surgical Association and the International Society of Surgery–American Branch; fellow of the American College of Surgeons; veteran of World War I; emeritus clinical professor at the University of Minnesota Medical School in Minneapolis; associated with the Charles T. Miller Hospital, St. Paul, where he was vice-president of the board of directors, Shriners' Hospital for Crippled Children, and the Veterans Administration Hospital in Minneapolis; died in St. Petersburg, Fla., March 11, aged 74.

FOREIGN LETTERS

INDIA

Methazolamide in Ophthalmology.—J. M. Pahwa (*Antiseptic,* vol. 57, January, 1960) stated that methazolamide, a carbonic anhydrase inhibitor, has actions similar to those of acetazolamide but is supposed to be more potent. The author treated with this drug a series of 49 patients who had eye conditions. The series included 36 patients with glaucoma, 5 with absence of the anterior chamber, 4 with cataract associated with a rise of intraocular tension, 2 who had corneal grafting, 1 with buphthalmos, and 1 with central serous retinopathy. In patients with acute congestive glaucoma the action was quicker when the drug was combined with local miotic drops.

It was most effective in controlling ocular tension in cases of recent onset and in patients with subacute and chronic congestive narrow angle glaucoma in whom a fair amount of vision remained. The effect was optimal in the first three days, and operation could be undertaken later on with safety. The drug was less effective in patients with nearly absolute or absolute glaucoma. In two patients in whom the tension could not be brought down quickly with methazolamide, acetazolamide gave prompt relief. The onset of action with methazolamide was delayed, but the effect was more prolonged. Two patients, in whom treatment with acetazolamide had to be discontinued because of the appearance of side-effects, were treated with methazolamide for three to four days and were operated on later with safety.

Six patients with chronic congestive glaucoma were given methazolamide. In two of these treatment with acetazolamide had to be discontinued because of side-effects. One had been operated on for glaucoma, but the tension was still elevated. Methazolamide helped to control the tension, thus obviating the need for further surgical treatment. Another patient failed to respond to both drugs and had to be operated on. Of 11 patients with simple primary glaucoma who were given methazolamide, 4 had already been operated on two or three times. The drug was ineffective in two patients with absolute glaucoma, while in others it proved helpful in controlling tension along with miotics used locally. It could be used for long-term therapy in these patients as the effect was prolonged. In patients with secondary glaucoma it proved valuable. One patient with aphakic glaucoma that had proved refractory to acetazolamide did well with methazolamide. Another who had hypopyon ulcer with secondary glaucoma and one who had exudative iritis also showed a good response.

It did not help a patient with thrombotic glaucoma and a child with buphthalmos. A patient with severe central serous retinopathy got no appreciable relief with this drug and suffered from such side-effects as depression and giddiness. Of five patients with absence of the anterior chamber two responded well. Two of the other three responded to acetazolamide and one did not respond to either drug. Side-effects with methazolamide were mild and consisted of malaise, depression, and fatigue. Gastrointestinal disturbances were less marked than with acetazolamide.

Tobacco and Oral Cancer.—Mody and Randive (*Indian J. M. Sc.,* vol. 13, Dec., 1959) reported that oral cancer is common in India and is associated with the habit of keeping a mixture of tobacco rubbed with slaked lime inside the mouth throughout the major parts of the waking hours. In order to determine the role of tobacco in the causation of carcinoma of the buccal mucosa, experiments were made on mice. Large-scale extraction of tobacco leaves was made with different solvents. The extracts were applied to the skin and painted on the buccal mucosa. Seven alkaloid-free extracts of tobacco were thus tested for their carcinogenicity. The solvents benzene and chloroform were tested on control groups of mice, and an untreated control group was also maintained. For comparison a standard carcinogen, 3:4 benzpyrene, was tested by the same methods on mice.

Histological examination of the painted skin and buccal mucosa was made to determine the changes, if any. All experimental mice were subjected to careful examination at autopsy, and the affected organs were studied histologically. Additional techniques included a test for screening carcinogens, tests of extracts containing alkaloids along with a cocarcinogen (croton oil), and testing with one subcutaneous injection a pure compound isolated from tobacco (gamma sitosterol) and alkaloid-free total alcohol extracts and alkaloid-free total water extracts. No definite carcinogenic changes were observed in the skin or the buccal mucosa. Some of the animals whose skins were painted showed hyperplasia of the epithelium, abnormal follicular changes, and chronic inflammation. A few of the

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he items in these letters are contributed by regular correspondents various foreign countries.

mice also showed hyperplastic buccal epithelium and thickening of the horny layer where the buccal mucosa was painted, but similar changes were seen with use of some of the solvents alone and in some normal groups of mice and could have been due to nonspecific irritation.

Tobacco probably acts as an irritant and could be carcinogenic. It may be that the life span of a mouse is not long enough to bring about true neoplastic transformation after the epithelial hyperplasia of the treated skin. With the standard carcinogen, 3:4 benzpyrene, the epithelium of the skin showed massive hyperplasia as well as epidermoid carcinoma, and the buccal mucosa proved refractory even to this substance, showing no definite carcinogenic changes.

The screening technique used for three tobacco extracts did not provide any evidence of carcinogenicity. Extracts containing alkaloids were painted on mice with the use of croton oil as a cocarcinogen. Within two months of painting advanced hyperplasia was seen, but the mice did not survive long enough for further observations. Many of the mice revealed interesting lesions of the internal organs which occurred in those treated with tobacco extract and those treated only with the solvent with about the same frequency. Mice who received subcutaneous injections of gamma sitosterol and three other tobacco extracts developed similar lesions in liver, lungs, and uterus. The mortality was high in the group receiving subcutaneous injection. The authors suggested further studies to determine the role of vitamin B deficiency and hormonal factors along with tobacco in inducing oral cancer. It might also be possible that the conversion product of tobacco which has been chewed slowly over long intervals in the mouth and has been thoroughly acted on by the saliva plays a significant role and deserves further investigation.

Hydrogenated Oils.—Studies conducted under the auspices of the Indian Council of Medical Research (*Mediscope,* vol. 2, Jan., 1960) to determine the effects of hydrogenated oils on consumers showed that such vegetable oils as groundnut oil, sesame oil, and their hydrogenated products with a melting point of 37 C (98.6 F) have almost the same nutritive value as butter. Hydrogenated oils have the same digestibility as nonhydrogenated oils. The hydrogenated oils influence the utilization of other dietary constituents such as calcium to the same extent as untreated vegetable oils and butter. Moreover, the butter and hydrogenated fats sold in India are good sources of vitamin A.

Short-term experiments on human beings indicated that butter, coconut oil, and hydrogenated oils tend to increase serum cholesterol levels, whereas vegetable and fish oils, rich in polyunsaturated fatty acids, lower these levels when they are high because of high fat intake. The increased level of serum cholesterol has been associated with atherosclerosis. A variety of factors can raise the serum cholesterol level. These include proteins, vitamins, and fats. Cholesterol levels tend to rise in persons who eat foods containing much fat or fats deficient in polyunsaturated fatty acids. The level tends to fall in persons on a low fat diet or a diet rich in polyunsaturated acids. The nature of the fatty acids in the diet has an effect on serum cholesterol levels.

Whether such changes in the diet can maintain such an effect for years and whether the cholesterol lowering effects are beneficial for patients with atherosclerosis or prevent occurrence of coronary heart disease are problems still open for investigation. Much of the evidence of a correlation between diet and atherosclerosis has been indirect and involves equating atherosclerosis with high levels of serum cholesterol. Therefore, while it is too early to arrive at a definite conclusion, it is wise to consume both butter and hydrogenated oils on the one hand and raw vegetable oils on the other in order to ensure an adequate intake of calories and polyunsaturated acids in the diet.

Spermicides.—Sharma and Saksena (*Indian J. M. Sc.,* vol. 13, Dec., 1959) studied the spermicidal action of sodium nimbidinate, a bitter fraction obtained from the seed oil of a tree known as Melia azadirachta Linn. or Azadirachta indica. It is believed to possess a diuretic action, while sodium nimbinate, a closely related salt from the same source, has been found to have spermicidal action. A sperm suspension was prepared from the epididymis of rats and from human semen, and 0.3 ml. of this suspension was treated with different dilutions of the drug in equal volume. Sperms were counted in a hanging drop preparation under the microscope after 5 and 30 minutes. The spermicidal activity on human semen was tested within 20 to 120 minutes after collection of the sample. To ensure uniformity of results only samples with adequate liquefaction time and a motility of 75% or higher were used. Analysis of results with rat's sperm suspension showed that 2.5 and 10.0% of the sperms were dead in control specimens after 5 and 30 minutes respectively.

The water soluble sodium nimbidinate in a concentration of 50 mg. per 100 ml. killed all the sperms in 5 minutes, while the concentration required to kill all sperms in 30 minutes was 2.5 mg. per 100 ml. The human semen usually showed highly motile sperms after 5 and 30 minutes in control samples. The lethal concentration of the drug for human semen was 1,000 and 250 mg. per 100 ml. in 5 and 30 minutes respectively. The authors preferred rat's sperm suspension from the epididymis, rather than from the testis, as the former is teeming with sperms and thus permits a more reliable evaluation of the spermicidal activity. Solutions of sodium nimbidinate were prepared in normal saline solution to avoid the lethal action of water on sperms. From the results it was concluded that a much higher concentration of the drug is required to produce spermicidal action in human beings than is required to produce such action in rats but that in view of the abundance and low cost of this product clinical trials would be desirable.

Blood and Plasma Volume in Pregnancy.—Vasavada and Wagh (*J. Obst. & Gynec. India*, vol. 10, Dec., 1959) studied three groups of patients to determine the changes in blood and plasma volume during pregnancy. The study included 29 women who were in the 32nd to 36th week of pregnancy, 10 in the 32nd to 34th week of pregnancy who were suffering from preeclamptic toxemia, and 18 gynecologic patients who served as controls. The average increase during pregnancy in plasma volume was 3.5 liters, about 15% above normal. The average blood volume in pregnancy was 5.7 liters, an increase of about 25%. In patients with toxemia the average plasma volume was three liters, which was less than that in the average normal woman. The blood volume (4.15 liters) also showed a decrease. The figures for plasma and blood volume in normal adults found in gynecologic patients were 3.2 and 4.6 liters respectively.

The average increase noted in this study during normal pregnancy was less than that reported by authors in the western hemisphere, whose figures for the average rise in plasma and blood volume were 30% and 40% respectively. Some of the normal pregnant women in this series had evidence of microcytic hypochromic anemia and hypoproteinemia, and the difference in the weight of Indian women and women in the western hemisphere may also be responsible for the difference in the average rise in plasma and blood volumes in pregnancy. This estimation should help in the treatment of obstetric patients, specially those suffering from anemia and toxemia in assessing the degree of deficiency.

Chlorpromazine in Labor.—Dass and Gaind (*J. Obst. & Gynec. India*, vol. 10, Dec., 1959) studied the effect of chlorpromazine on 138 patients in labor. In 97 other women (control series) no chlorpromazine was given. The patients in the trial group were given 25 mg. of chlorpromazine by mouth followed by an injection of 50 mg. of meperidine when labor was considered to be well established. An intramuscular injection of chlorpromazine was given only if the patient was still restless after oral administration of the drug. Both chlorpromazine and meperidine were given again after four hours if necessary. Control group received 100 mg. of meperidine intramuscularly along with injection of 0.12 Gm. of phenobarbital when moderate labor pains had set in. A mixture containing potassium bromide and chloral hydrate was given every three hours. Meperidine and phenobarbital were given every four hours as required.

In five of the patients in the trial group labor came to a standstill with disappearance of pains, and in another eight patients labor was too advanced to allow any correct opinion about the effect of the drug. Of the rest, 99 patients required only 25 mg. of chlorpromazine and 50 mg. of meperidine, 9 required a second dose, 15 had to b given intramuscular doses in addition to oral doses of chlorpromazine, and 2 required 75 mg. of chlorpromazine. Among the controls, 86 required only one injection of meperidine and phenobarbital, 2 required larger doses of meperidine, and 33 required additional trichloroethylene anesthesi Most of the patients in the control groups receive 100 mg. of meperidine, while those in the tri group required only 50 mg. About 21% in bot groups required larger doses.

The patients who received chlorpromazine we much quieter, more cooperative, and require smaller quantities of trichloroethylene than the co trols, and the amount of meperidine required w reduced by 50%. No excitement and restlessne was noticed in any of the patients receiving chlo promazine, although some authors have report such effects. The duration of labor was definite shortened after the administration of chlorprom zine. In over 53% of these patients labor lasted hours or less, while in the control group only 36. of patients had a similar duration of labor. T difference was significant, as the trial group c tained a larger number of primiparas. The short ing of the duration was not due to an increase the strength of uterine contraction but probably its action on the hypothalamus, for the patie appeared relaxed, restful, and indifferent to labor pains.

The complication of uterine inertia and the sultant prolongation of labor was not common, though it has commonly been found by others w used larger doses of chlorpromazine. The analge and sedative effect of the other drugs was mu better after the addition of chlorpromazine. A larg percentage of patients in the trial group than in t control group were willing to have another chi There was satisfactory analgesia without amnes because of the small doses used. The calming effe of the drug improved uterine contractions indirec ly. Only 29 patients had difficulty in recollecti the labor, and most of these had received a secon dose. The need for forceps in the trial series showe very little increase, and other obstetric abnormal ties did not increase. Breech extractions, repair the perineum, and application of low forceps we much easier, as the patient required only a sma amount of inhalation anesthetic. The duration the third stage did not vary significantly in the tw groups. The incidence of postpartum hemorrhag was less in the trial group; four of the control group required blood transfusion and in two the placenta had to be removed manually, but these procedures were not necessary in any patients in the trial group. Their general condition was better, serious vomiting was absent, and there was no dehydration or exhaustion.

Eleven of the trial group had mild vomiting. Eighteen in the control had this complication, and in five of them it was severe enough to require intravenous replacement of fluids. Other side-effects of chlorpromazine were drowsiness, giddiness, pallor, sweating, and general flaccidity, but these were transitory. None of the patients showed a significant fall of body temperature. No effect of chlorpromazine was noticed in the infants. On the whole chlorpromazine was found to be useful when given with care. It potentiated the action of meperidine and made it necessary to use only half the former dose. No adverse effects were noticed in mothers given these doses or in their babies.

Needle Biopsy of Lung.—Sarin and Bhatnager (*Indian J. M. Sc.*, vol. 13, Nov., 1959) examined lung biopsy specimens from nine patients with lung disease in whom the diagnosis could not be made by examining the sputum or by bronchoscopy. The right side of the chest was involved in six patients and the left in three. The biopsy, which was the only way to clinch the diagnosis, proved safe in all but one patient, who developed hemoptysis after the biopsy. This was, however, easily controlled. Six of the nine patients had carcinoma of the lung, one unresolved pneumonia, one extensive fibrosis, and one tuberculosis with caseation.

Blood Histamine and Skin Sensitivity.—In an attempt to determine the cause of tropical eosinophilia Jha and Sinha (*Indian J. M. Res.* 48:41 [Jan.] 1960) estimated the histamine content of whole blood and tested the skin sensitivity to histamine, the blood histamine level being known to rise in anaphylactic reactions and allergic disorders. The 58 patients studied had typical clinical manifestations of tropical eosinophilia, with or without a history of a previous attack, and had an absolute eosinophil count of 3,000 or more per cubic millimeter. Control studies of 12 normal persons with an absolute eosinophil count of less than 750 per cubic millimeter, and without a history of previous allergic manifestations, were made.

In both groups stools were examined for helminths and protozoa. Sputum specimens were examined for acid-fast bacilli and eosinophils, and the chest was examined radiologically. The histamine sensitivity test was done by iontophoresis. The control value for blood histamine level was found to be 0.0566 mcg. per milliliter. The values in the 58 patients varied from 0.076 to 0.459 mcg. per milliliter (average 0.230). Thus the level was about five times higher than the normal. There was no correlation between the histamine level in blood and the absolute eosinophil count.

The skin sensitivity test was made in 8 normal subjects and 27 patients with tropical eosinophilia. All the controls had a normal reaction except one who showed a moderately positive reaction, whereas 25 of the patients tested had a markedly or highly positive reaction and in the other 2 it was moderately positive. Although eosinophils are known to have a high content of histamine, the high blood histamine level in these patients could not be so explained as there was no parallelism between the absolute eosinophil count and the blood histamine content. It might, however, be due to release of histamine from tissues, which is known to happen in allergic and anaphylactic reactions. The increased blood histamine level and increased skin sensitivity to histamine as found in this study supported the allergic theory of the cause of tropical eosinophilia. An increased liberation of histamine might be responsible for the clinical manifestations of this condition, and the increase in number of eosinophils might be secondary to the increased blood histamine level. The eosinophils might be concerned with the detoxification of histamine rather than its elaboration.

The Spleen in Drug-Resistant Leishmaniasis.—Sen Gupta and Chatterji (*J. Indian M. A.* 34:81 [Feb. 1] 1960) reported that four patients with visceral leishmaniasis who had failed to respond to antimony and aromatic diamidine compounds were subjected to splenectomy. The duration of illness in these patients was four to five years. Macroscopic changes consisted of massive enlargement of the spleen (which was firm in consistency), thickening of the capsule, dark red cut surface, and prominent trabeculae.

The histological changes were those usually associated with advanced leishmaniasis with certain additional features. There was marked infiltration of the splenic pulp with parasitized and nonparasitized histiocytes, numerous plasma cells, and some lymphocytes leading to attenuation of most of the malpighian corpuscles. The vascular bed showed marked dilatation and congestion and was enormously increased. The supportive connective tissue was thickened and increased. The sinusoids contained numerous phagocytic cells, in many of which Leishman-Donovan bodies and erythrocytes were found. The pulp contained leishmanial granulomas consisting of giant cells, epithelioid cells, or histiocytes with or without leishmaniae surrounded by masses of plasma cells and some lymphocytes. Evidence of reactive hyperplasia was present in the form of occasional lymphoid follicles, although most of these were atrophic. Hemosiderotic nodules were present in two patients and hemopoietic foci were also seen.

The response to leishmanial infection was by proliferation and accumulation of histiocytes, plasma cells, and a few lymphocytes. The presence of granulomas was additional evidence of the chronic inflammatory process due to the leishmanial infection. The reactive hyperplasia could be compensatory. The occurrence of splenomegaly with vascular congestion persisting for a long time led to periarterial hemorrhages and production of siderotic nodules. The presence of hemosiderin granules in the macrophages could be due to increased blood destruction, repeated transfusions, or both. The hemopoietic foci probably represented a nonspecific phenomenon related to interference with or inadequate hemopoiesis in the marrow.

Arginase Inhibitor for Uremia.—D. K. Sen (*Indian J. Surg.* 21:514 [Dec.] 1959) stated that the present methods of treatment of renal type of uremia are based on the principle of eliminating urea from the body and that none of them give satisfactory results. The patients die of salt depletion when intestinal dialysis, peritoneal irrigation, or artificial kidney are used. The author tried to inhibit urea synthesis in the body and thus prevent urea retention. Arginase activity is essential for the synthesis of urea. Administration of a substance which would inhibit the activity of arginase should lead to complete stoppage of urea formation. L-lysine monohydrochloride is a most powerful arginase inhibitor in vitro. When given intravenously, it does not lead to any untoward side-effects and does not cause any significant increase in the amino acid pool. The effect of this amino acid was therefore assessed in dogs and human beings with uremia.

When uremic dogs were given 1 Gm. of L-lysine HCl in 10% solution daily, the increase in urea level was only 3 or 4 mg. every 24 hours, and the dogs survived much longer (274 to 278 hours after the operation), than the controls. Increasing the daily dose of lysine to 1.5 Gm. a day did not produce any further improvement in the results. Administration of lysine to normal dogs where no bilateral nephrectomy was performed resulted in some reduction of the urea level, but a minimal urea level was still maintained. Intravenous injections of 1 Gm. of L-lysine HCl in three patients who had developed postoperative uremia resulted in a rapid fall in the blood urea level and simultaneous improvement in the clinical state. Thus the results of administration of this amino acid to dogs and human beings with uremia were satisfactory. Even in patients with prerenal and postrenal uremia, in whom the causes should be eliminated, administration of lysine would help in reducing urea synthesis to a minimum until the causative factors are corrected.

Helminthiasis.—Pohowalla and Singh (*Indian J. Pediat.*, vol. 26, Dec., 1959) studied a series of 1,722 infants and children below the age of 5 years to determine the incidence and nature of worm infestation. Of these 23.3% were found to be infested with one or more types of worm. A steady rise in the incidence of this infestation was correlated with the age of the children. It was 1.1% in the first year and 48.4% in the fifth year. Only seven children showed adult worms in stools on macroscopic examination. Ascariasis was most common and thread worm infestation the next most common. Trichiuris trichiura and Hymonelopis nana were found in small numbers, and the absence of hookworms was conspicuous. Less than 50% of the children with worms had symptoms referable to the gastrointestinal tract which were not entirely attributable to the infestation itself. Of those who had intestinal complaints 75% did not show the presence of worms. Of those with ascariasis 43.1% gave a history of having passed roundworms previously, most of the rest gave no history of passing any worms, and 12.8% had passed threadworms. Only 14% of those with threadworm infection gave a history of passing these worms; 63% gave no such history; and 23% had at one time passed roundworms.

Thirty-three children had multiple infections, the commonest of which were roundworms and threadworms together. The infection was asymptomatic in many of these children. In this series 727 children were underweight due to malnutrition. Of these only 22.33% had worm infestation, while of the 995 who were adequately nourished 22.6% had worms. Thus no difference was seen in the incidence of worm infestation in well-nourished and malnourished children. Worm infestation was not an important contributory cause of malnutrition. No relationship was observed between the occurrence of convulsions and worm infestation. The authors warned against attributing convulsions in children to worm infestation.

Revascularization of Heart.—H. K. Kamdar and co-workers (*Current Med. Pract.*, vol. 4, Jan., 1960) investigated the value of bilateral internal mammary artery ligation in the treatment of coronary artery disease through experimental work on dogs. They compared the degree of protection offered by internal mammary ligation with that offered by ligation of the anterior descending branch of the left coronary artery and the presence or absence of extracoronary anastomosis between pericardiophrenic artery and myocardial vessels after such ligation by dye infections. In seven dogs who served as controls, the anterior descending branch of the left coronary artery was ligated when the patient was under anesthesia. All these dogs died within 2½ days of the operation. Those who lived for 2½ days had hurried respiration and lay passively. The electrocardiogram (ECG) in two of these dogs showed evidence of anterior myocardial infarction in one and ventricular fibrillation in the other. Autopsy of four dogs showed no infarct in three, who died within 40 minutes of ligation, while histological examination in the fourth dog showed an early myocardial infarct.

In 10 dogs who were protected, the internal mammary artery was ligated on both sides in the third intercostal space two weeks before the anterior descending branch of the left coronary artery was ligated. Four of these dogs died. The ECG in one of the dogs who died showed ventricular fibrillation, and this was probably the cause of death in the other three dogs also as they died within 45 minutes of ligation. The surviving dogs had hurried respirations and lay passively for some time and then became normal again. Thus they all showed signs of coronary occlusion. The ECG in four of the surviving dogs showed evidence of an anterior myocardial infarct. Histological examination of the heart in dogs who died early showed no evidence of infarct. The surviving dogs were sacrificed later, and histological examination showed evidence of early healing and healed infarct. Thus previous ligation of the internal mammary arteries appeared to have a protective effect on subsequent ligation of the descending branch of the left coronary artery.

Convulsions.—N. R. Bhandari studied 100 consecutive cases of convulsions in children below the age of 12 years (*Indian J. Pediat.* 26:477 [Dec.] 1959). The maximum incidence for any single year of life occurred in the first year; 36 were less than one year old. The commonest cause, fever, was present in 38 of the patients, most of whom were between 6 months and 2 years of age. Of these 36 had respiratory infections. Fourteen of the 38 had a history of convulsions. These children are likely to develop epilepsy in later life. The second largest group (16) suffered from idiopathic epilepsy. Another 16 had meningitis and of these 12 had tuberculous meningitis.

Ten patients had encephalitis; seven had hypocalcemic infections, with radiographic evidence of rickets in four; five had mental retardation; and three had pyridoxine deficiency, which was shown by urinary saturation studies. No other cause of convulsions could be found in them. One of these had marked anemia and the other two moderate anemia; two were less than 6 months old and were totally breast fed. All three were underweight, and all responded promptly to intramuscular injections of vitamin B_6. No relapse occurred during the period of hospitalization. One child in the series had a space-occupying intracranial lesion and another had hydrocephalus. Birth injuries were probably responsible for the convulsions in a 20-day-old infant. One child had crowing convulsions, and one developed convulsions after a scorpion bite. The seizures lasted 3 to 10 minutes in most. In 91 they were generalized.

Infantile Hepatic Cirrhosis.—Berry and Sainani (*J. Indian M. A.* 34:121 [Feb. 16] 1960) studied a series of 41 infants between 1 and 3 years of age who had infantile hepatic cirrhosis. They observed that, although no definite cause was common to all, malnutrition due to an unbalanced diet, virus infection, or both could be responsible but that congenital syphilis and helminthiasis did cause cirrhosis. Thirty-two were from orthodox vegetarian families, but only nine belonged to poorer class. The rest came from middle-class families. The onset was insidious in all, with anorexia, gastrointestinal disorders, irregular fever, irritability, and abdominal swelling. Jaundice, swelling of the feet, and a markedly distended abdomen were late features. The incidence of this disease was maximal in the first born, and the frequency decreased as the number of children increased. Four infants had older siblings with a history of liver disease. All of the older siblings had died of it. A tendency of the disease to run in successive children in a family has been observed by others where some sort of infection acquired from the mother has been blamed. Such a history was present in only four patients in this series, and none of the mothers had suffered from jaundice during pregnancy.

Rescinnamine.—Datey and Kurien (*Current M. Pract.* 4:15 [Jan.] 1960) studied the effect of rescinnamine on eight patients with mild to moderate hypertension and grade 1 to grade 2 retinal changes. One patient had malignant hypertension and received pentolinium tartrate in addition to rescinnamine. The ages of these patients varied from 20 to 58 years, and the duration of therapy was from 2 to 16 weeks. The drug was given three times a day, the total daily dose being 0.75 to 4.00 mg. (average 2 mg.). Of the eight patients six registered a fall in blood pressure. The average blood pressure before therapy was 195/115 mm. Hg and after treatment 165/95 mm. Hg. None of the patients developed postural hypotension. Only one patient showed evidence of tolerance. The authors found this drug useful in patients with mild to moderate hypertension. It is less potent than reserpine, but the incidence of side-effects is low.

UNITED KINGDOM

Social and Preventive Medicine.—An annotation in the *British Medical Journal* of March 12 referred to the annual reports of the London School of Hygiene and Tropical Medicine. It seemed novel to observers from overseas that the police were looked on as advisers whose help was sought in almost any problem, ranging from lost canaries to marital arguments. Much of the work of the police was found to stem from such medicosocial problems as homosexuality, prostitution, aggressive behavior, and truancy. Police and social workers emphasized that discharged prisoners and patients recently discharged from mental hospitals cause many of their problems.

Another interesting finding described in the report was that of the Department of Human Nutrition, which was asked to investigate the dietaries of a number of hospitals in West Cornwall. The department found that the structure of the dietaries was faulty and that "plate waste" was sometimes excessively high. They concluded that, because of the difficulties inherent in hospital catering, it was doubtful if the best of existing arrangements would ever be entirely satisfactory from both the catering and nutritional points of view. Rather than provide an individual service for each hospital, it might be better to use modern equipment and techniques to prepare meals in centers and to hold them in deep-freeze units until shortly before they are to be served to the patients. The meals could be quickly heated in a ward kitchen and served in the manner now customarily practiced in airplanes.

The report gives the findings of a group who studied the effect of footwear on health. They found the high incidence of acquired foot defects was mainly caused by badly fitting shoes. This was the fault of the manufacturers for producing designs which, on physiological grounds, were bad and had insufficient graduations in size and shape and the fault of the retailers for insufficient training of sales staff. It is also the responsibility of the wearer to acquire more education on the subject. The misery resulting from unsuitable footwear will persist until persons demand shoes which fit, are functional, and support the feet. At the same time such shoes could be attractive in appearance.

Menstrual Hormone.—An annotation in the *British Medical Journal* of March 19 stated that the idea that menstrual blood is something more than ordinary blood and that it contains substances of which the body must rid itself must be very old. The first serious scientific work on menstrual toxin is probably that of O. W. Smith, although comparatively little attention has been paid to her views. Recent work, based on sound and accepted pharmacological principles, has shown the presence of slowly acting plain-muscle stimulants in human endometrium and has provided evidence that these or similar substances not only appear in menstrual blood but also circulate in the systemic blood during menstruation.

The active agents are lipids whose pharmacological behavior is such that they cannot be classified as acetylcholines, histamines, or 5-hydroxytryptamines. They are probably long-chain fatty acids. V. R. Pickles studied the myometrial responses to extracts of menstrual fluid and found that human myometrial strips and the guinea-pig uterus are stimulated in vitro, while intravenous or intracardiac injections in the guinea-pig cause uterine contractions in vivo. The response of human myometrial strips may consist of coordinated contractions of the same frequency as the normal menstrual contractions of the uterus described by H. Hinselmann and by H. Schroder. It is suggested that these are responsible for the expulsion of menstrual fluid.

Additional evidence suggesting a physiological role of these substances comes from the fact that they can be detected in premenstrual, but not in preovulatory, endometrium and have been found in the circulating blood during menstruation but not eight days later. Pickles suggested that the normal contractions of the menstruating uterus may be explained as myometrial responses to a substance with the properties of the menstrual stimulant which pass from the endometrium to the myometrium, either by some local route or through the general circulation. It is possible that this mechanism could also be the basis for the abnormal contractions which occur in dysmenorrhea. In this respect it is perhaps striking that the most sensitive human myometrial strips used by Pickles came from a 44-year-old patient's uterus which had been removed because of incapacitating dysmenorrhea.

New Drugs for Leprosy.—At a meeting of the Royal Society of Tropical Medicine and Hygiene in London, trials with new drugs for the treatment of leprosy were discussed. Dr. Davey compared the bacteriological response (plotted as the bacterial index) to a new drug with the average response obtained from the accumulated experience in a large number of patients receiving diaminodiphenylsulfone (DDS). He described how a new thiourea derivative, Ciba 1906, had been extensively studied at the Leprosy Service Research Unit, Uzuakoli, Nigeria, and said that it was found to be as active as or slightly more active than DDS. In doses of 3 Gm. daily by mouth, the drug produced no toxic symptoms or lepra reactions, but if given over long periods there was evidence of drug-resistance between the 36th and 44th month. It is advised that Ciba 1906 should not be given for more than two years. The drug is particularly useful in those patients who are hypersensitive to DDS.

The results of trials with another drug, Etisul (diethyl dithiolisophthalate), are also promising. It can be administered by inunction. Its objectionable smell can be masked. When Etisul alone was given the improvement was greater than with DDS for the first four months, but then resistance appeared. The current trials suggested that Etisul in combination with Ciba 1906 or DDS produces improvement for six months or more and that the results are superior to those obtained with the two latter drugs alone. The activity of Etisul is probably due to the release of ethyl mercaptan.

CORRESPONDENCE

THE SMOKING CONTROVERSY

To the Editor:—Congratulations on the publication of the recent article "Statistics and Tobacco."[1] It is either the first or one of the first published by THE JOURNAL giving the fallacies in some of the data used to support an alleged relationship between smoking and lung cancer. Science itself and the attitude of the public to scientific problems will correctly develop only when both sides of a problem are presented. To correctly interpret scientific data, it is necessary to give equal thought to those findings that seem to be in opposition to one's own views. A few recent observations will show the necessity for continued scientific evaluation of the problem of the rising incidence of lung cancer.

There is no significant correlation between the amount of tobacco consumed and the death rate from cancer of the lung in the United States.[2] In England and Wales the number of deaths attributed to cancer of the lung over the last 25 years has been much greater than the increase in tobacco consumption.[3] There is, however, a significant correlation in the United States between the ratio of population to physicians and the ratio of population to beds and the number of reported deaths from cancer of the lung.[2] The number of deaths from cancer of the lung in each county in Texas is related to the number of doctors and the number of hospital beds.[4] Therefore, better diagnoses, decrease in the number of deaths from infectious diseases by both prevention and therapy, and the increase in the percentage of older persons in the population seem to be more significant factors to account for the apparent increase in the frequency of carcinoma of the lung than any one carcinogen or group of carcinogens.[2]

Every physician knows that coronary occlusion is a frequent cause of death in a person with hypertension. The statistical relation between smoking and hypertension and smoking and coronary occlusion is most interesting. The death rate from coronary heart disease among regular users of cigarettes is 63% higher than the rate for non-smokers, but the death rates from hypertension, cerebral vascular lesions, chronic nephritis, and chronic rheumatic heart disease are no higher for heavy than for light smokers.[5]

Hammond[6] has made the following statement. "It is not certain why the death rate of cigar and pipe smokers was lower than the death rate of cigarette smokers. However, it is reasonable to suppose that tobacco smoke is more likely to have an effect upon a person who inhales the smoke than upon a person who does not inhale the smoke." Doll and Hill,[3] statisticians of equal renown, observed that "it would appear that lung-carcinoma patients inhale slightly less often than other patients." Cornfield and associates[7] point out that this is contradictory to the relationship between smoking and lung cancer. Why do most heavy cigarette smokers fail to develop lung cancer if cigarettes are in fact a causal agent? In our study of smoking and disease,[8] 97.2% of the white men who had smoked cigarettes for 16 years or longer did not have lung cancer at the time of the survey, according to the medical records.

Although condensed tobacco smoke contains substances that are carcinogenic for mouse and rabbit skin, it does not necessarily follow that these substances are also carcinogenic for human lungs nor does it follow that they are not.[7] The experimental production of cancer of the skin of animals smeared with tobacco smoke condensates does not in itself prove that cigarette smoking is a direct cause of lung cancer.[6] When an agent has been shown to be carcinogenic for rabbits as well as for several different inbred strains of mice, there is reason, according to Hammond,[6] to suppose that it is probably carcinogenic for other species, including man. Anyone familiar with the biologic action of carcinogenic agents recognizes the fact that different tissues within the same animal may respond differently to the same carcinogen. I have produced multiple tumors in the lungs of white Pekin ducks with methylcholanthrene but have not observed any tumors when the same agent was put into the esophagus.[9]

In 1959 it was stated by members of the Public Health Service[7] that "the vital statistics and necropsy data that support the presumption of a real increase in lung-cancer risk certainly apply to the years after 1920" and that "because of the uncertainties associated with changes in diagnostic accuracy, no firm conclusions can be reached on whether the rate of increase in lung-cancer mortality has, in truth, accelerated since 1920." The chief[10] of the epidemiology section of the National Cancer Institute recently pointed out that the "International Lists of Causes of Death" did not separately list cancer of the lung and pleura, or even cancer of the respiratory system as a whole, until the fourth revision, first used in 1930. Prior to 1930 the term bronchogenic carcinoma was lumped with 90 other cancers of various sites. Between 1930 and 1938, when this diagnosis appeared on a death certificate it was tabulated with cancer and other malignant tumors of other respiratory organs, that is, with tumors other than those designated as larynx or as lungs and pleura. It was not until the fifth revision came into use in 1939 that deaths which physicians charged to bronchogenic carcinoma were separately identified in official statistics. A variation does occur in the interpretation of scientific data within the Public Health Service, as I pointed out in the congressional hearing [11] and as was cited by Berkson in THE JOURNAL.[1] This governmental agency should not be criticized because there are differences of opinion among its members, but these facts should be given to the public when these opinions have been arrived at by responsible investigators.

Cutler [12] in 1955 summarized 14 retrospective studies on lung cancer and smoking and showed that the estimate of relative risk of smokers and nonsmokers for developing lung cancer varied from 1.2 to 36.4 for all smokers and from 1.9 to 79.0 for heavy smokers. It is inadvisable [13] to convert a pipe and cigar smoker into a statistical cigarette smoker by considering a cigar equal to five cigarettes and a pipeful of tobacco equal to two and one-half cigarettes as Doll and Hill [3] did, nor is it advisable to consider one cigar the equivalent of 10 cigarettes and one-half can of pipe tobacco or more the equivalent of 21 or more cigarettes as Sadowsky and others [14] did.

In 1958 Lilienfeld, [15] in studying the differences between smokers and nonsmokers, observed that cigarette smokers marry more often, move more frequently, change jobs more often, are hospitalized more often, and participate in more sports than nonsmokers do. Also, the parents of nonsmokers are more often foreign born than those of smokers. "The degree of difference," according to Lilienfeld, "between smokers and nonsmokers was not sufficient to account for the high degree of association between cigarette smoking and lung cancer and therefore could not influence the causal inference derived from this association, though it might be sufficient to explain the association of cigarette smoking with peptic ulcer and coronary artery disease."

It was found in Scotland in 1958 that women who were in paid employment and those who were occupied only with household duties did not differ significantly in their smoking habits. [16] Men who were not churchgoers were more likely to smoke heavily, and "men who took alcohol regularly—i. e., at least once a week—were much more likely to be heavy smokers." Probably the most significant fact that emerged from their analysis, according to the Scottish investigators, was that "over half of the men started to smoke in their first job when they had newly achieved the status of wage earners." Furthermore, "the lower the social-class level, the higher the ratio of smokers to nonsmokers, the greater the proportion of heavy smokers, and the earlier the age at which regular smoking began. Further evidence of the connection between nonsmoking and 'middle-class respectability' was provided by the association of nonsmoking with abstention from alcohol and with church attendance."

The study [17] made in 1958 by the staff of the American Cancer Society on cigarette smoking among high school students includes the following observations. 1. Parental smoking behavior is significantly related to the smoking behavior of high school students. 2. The smoking behavior of boys tends to conform more closely to that of the father, whereas the smoking behavior of girls follows more closely that of the mother. 3. If one parent has stopped smoking and the other continues to smoke, the proportion of students who smoke is somewhat higher than in families in which neither parent smokes but remains lower than the proportion in families in which both parents continue to smoke. 4. In families in which the father smokes, but not cigarettes, and the mother smokes cigarettes, the percentage of smokers among the children is about the same as in those families in which both parents smoke cigarettes. 5. The percentage of smokers is higher among students in parochial high schools than in public city high schools. 6. The percentage of smokers in a family is inversely related to the educational level of the parent. 7. In families of parents of little education smoking is taken up at an earlier time, but the educational level does not affect whether or not smoking is eventually taken up within the high school years. 8. The percentage of smokers is higher among students who have taken or are taking general mathmatics rather than algebra.

These scientific observations indicate that much more study is needed in order to clarify the questions regarding smoking and lung cancer.

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ADDITIONAL COMMENTS ON LUNG CANCER

To the Editor:—In connection with the reservations expressed editorially (*J. A. M. A.* 171:2104 [Dec. 12] 1959) regarding the causal relationship between cigarettes in smoking and lung cancer presented by the Surgeon General of the Public Health Service (*J. A. M. A.* 171:1829 [Nov. 28] 1959) and the questions raised by Berkson (*J. A. M. A.* 171:967 [Feb. 27] 1960), attention is directed to a report just issued by the World Health Organization (Epidemiology of Cancer of Lung: Report of Study Group, WHO Technical Report Series, no. 192, Geneva, 1960). The study group members were Richard Doll and R. E. Waller of England, Harold F. Dorn and Morton Levin of the United States, Leiv Kreyberg of Norway, Erkki A. Saxen of Finland, Daniel Schwartz of France, M. Segi of Japan, and L. M. Shabad of U.S.S.R. Dr. Doll was the chairman and Drs. Dorn and Levin were corapporteurs. The meeting was held in Geneva on November 16 to 20, 1959.

In section 3.1, page 4, of the report which deals with cigarette smoking, the following statement is made. "The Study Group unanimously agreed that there was no reason to modify the conclusions reached by [previous] experts that the sum total of the evidence available today was most reasonably interpreted as indicating that cigarette smoking is a major causative factor in the increasing incidence of human carcinoma of the lung. Recognizing that this conclusion has not been accepted by all who have studied or written on the subject, the Study Group agreed that while some of the criticisms levelled did suggest avenues for further investigation, none could be considered as casting any serious doubt on the conclusions reached on the basis of the extensive studies already made."

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CYTOLOGICAL SCREENING

To the Editor:—The editorial, "Cytological Screening Techniques," in The Journal, March 12, page 1165, is a well-intended and effective statement in behalf of an exceptionally worthy project, the increased use of cytological screening for uterine cancer. It would seem desirable to add one more thought. The pathologist, whose trained eye and judgment are so kindly recommended for counsel in subsequent steps, has also a useful role in the cytological step. Problems in interpretation and correlation of smear and biopsy findings are frequent and unpredictable. The solution of these problems can often be expedited or even more safely assured by close counsel between the attending physician, a pathologist whom he knows personally and understands, and the pathologist-supervised screener.

Accordingly, to balance the well-taken point that "mail-order" screening puts cytology within reach of all physicians, it might be added that this reassuring thought need not obscure the potentially greater advantages of using local, properly supervised screening facilities where they are available.

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DETACHABLE LABELS ON SAMPLES

To the Editor:—How long will it take various drug companies to use detachable labels on their samples? We are deluged with samples, and many have a good deal of value but have labels which, so to speak, require a "crowbar" to get them off. I throw samples with such labels in the wastebasket in disgust. The Journal might publish this in the hope that someone will take the hint.

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PHYSICIAN WHO WAS NOMINATED FOR PRESIDENT

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[illegible] founding of this Republic, numerous [illegible] of the American medical profession have [illegible] high public office, but never the highest. In addition to their customary functions as state and city health commissioners, physicians have served as mayors of cities, as governors and legislators of states, as members of Congress, as cabinet officers, and in one instance as a justice of the Supreme Court.[1]

In contrast to the situation in the Central and South American nations, where medical men frequently have been chief executives (as in Brazil today), no president of the United States has had a medical background. No presidential candidate chosen by a major political party has been a physician, but on one occasion a prominent member of the profession sought and almost achieved the nomination.

The interesting event occurred 40 years ago, in 1920, when Major Gen. Leonard Wood came to the Republican national convention with more pledged delegates than any other candidate. He held the lead for a number of ballots, but never was able to muster more than 314½ votes, about half the required total. Out of this unfortunate deadlock emerged a dark horse, an attractive but relatively obscure senator from Ohio named Warren G. Harding, who was nominated and overwhelmingly elected. General Wood also had been proposed for the presidency in 1916, but in that year the nomination went to Charles E. Hughes, who was narrowly defeated by the Democratic incumbent, Woodrow Wilson.

Leonard Wood, born in Winchester, N. H., on Oct. 9, 1860, received his M.D. degree from Harvard Medical School in 1884. After an unsuccessful and frustrating year of private practice in Boston, he decided to enter the U. S. Army, but at that time the only available appointment was as a contract surgeon in Arizona, which he accepted. In 1886 he was commissioned first lieutenant in the medical corps and proceeded to distinguish himself in the Apache uprising, so much so that he was awarded the country's highest military decoration, the Medal of Honor.

In 1891 Dr. Wood was promoted to captain and in 1895 was transferred to Washington, D. C. Here he counted President and Mrs. McKinley among his patients, and here he became friendly with an active Assistant Secretary of the Navy named Theodore Roosevelt.

When the war with Spain broke out in 1898, Teddy Roosevelt promptly organized the first U.S. volunteer cavalry, popularly known as the Rough Riders, with Wood as colonel and himself as lieutenant colonel. This colorful unit saw action at Las Guasimas in Cuba in June and shortly thereafter at San Juan. Wood was brevetted as brigadier general and in October became military governor of disease-ridden Santiago. In December, now a major general of volunteers, he was appointed military governor of Cuba, a position he held until May 20, 1902, when Cuba reverted to the Cubans.

In February, 1901, President McKinley promoted Dr. Wood from his permanent rank of captain in the Army to brigadier general, despite vociferous complaints from his many seniors and some hostility in the Senate. Another favored officer who received similar advancement, in 1906, was Captain John J. Pershing, who was promoted by President Roosevelt to brigadier general over 862 senior officers.

During Dr. Wood's tenure as governor of Cuba his engineers made Havana the cleanest city in the world. This feat reduced the incidence of typhoid and other enteric diseases, but the ubiquitous yellow fever and malaria continued to flourish. When the Yellow Fever Commission, directed by Major Walter Reed, arrived in Cuba in 1900, General Wood ardently supported this work which, at the cost of the life of Dr. Jesse W. Lazear, proved that yellow fever was transmitted by the mosquito now known as the Aedes aegypti. When Col. William C. Gorgas applied this knowledge in Havana, yellow fever was conquered there, as it was later in Panama.

After service in the Philippines, Dr. Wood, promoted to major general in 1903, was called to Washington in 1910 to become Chief of Staff. In this office he had to contend with the strongly entrenched position of another former medical officer, the Adjutant General, Major General Fred C. Ainsworth, who had entered the Army in 1874 in the Medical Corps. Ainsworth was retired in 1912, and for the next two years General Wood reigned supreme.

At the end of his four-year term as Chief of Staff, General Wood became commander of the Department of the East. World War I had begun in Europe, and Wood, foreseeing our eventual entry into this conflict, organized the officers' training center at Plattsburg, N. Y., which the Roosevelt boys and many others attended. When the United States entered the war in April, 1917, he was the senior officer in the Army and hoped for, and deserved, a command in Europe. He trained the 89th Division in Kansas, but was abruptly removed from his command just as the division was about to embark. He then trained the 10th Division, while General Pershing took command of the American Expeditionary Force.

This harsh treatment of General Wood by President Wilson and Secretary of War Baker made Wood more of a public figure than ever. Although he had been passed over for the Republican nomination for president in 1916, he was a very active candidate in 1920, but lost out in the smoke-filled room. In 1921 President Harding sent him to the Philippines as governor general, where he served with distinction until his death on Aug. 7, 1927. He died in Boston after the third operation for a tumor of the skull, due to an accident in Santiago, Cuba, about 30 years earlier.

Those of us who had the privilege of meeting General Wood, remember him as a stalwart, athletic man, with a massive head. He walked with a rolling gait, because of partial paralysis on the left side. He was a convincing, if not eloquent, speaker. It is interesting to speculate what might have been the course of American history had he become president, and who might have succeeded him had he died in office during a second term. Certainly he would have been a strong president, which unfortunately cannot be said of the gentleman who was elected in 1920.

Reference

1. Tobey, J. A.: Physician Who Served on Supreme Court, J. A. M. A. **170:**109 (May 2) 1959.

PRACTICES RELATING TO NURSES FROM ABROAD

Statement by the American Nurses' Association

As the professional organization for registered nurses in this country, the United States member of the International Council of Nurses, and an official sponsor of the Department of State's Exchange-Visitor Program for Nurses, the American Nurses' Association (ANA) is concerned about practices relating to foreign nurses in this country under the Exchange-Visitor Program or on immigration visas.

The ANA strongly commends and supports the purposes and objectives of the Exchange-Visitor Program as outlined in the Information and Education Act of 1948. The basic aim of the Exchange-Visitor Program for Nurses is to afford educational experience for nurses to help them improve their knowledge and skills which will be useful when they return to their own countries and, by providing them such experience, to promote better understanding of the United States. Aware of the values of this program, the ANA recognizes the need to safeguard its purposes and objectives and, at the same time, to protect the practice of nursing in the interests of the public.

Many complaints about abuses of the Exchange-Visitor Program for Nurses have come to the attention of the American Nurses' Association. Among such reported abuses are the following: misleading advertisements which promise, but do not fulfill, planned educational experience for foreign nurses; inadequately supervised programs; employment of foreign nurses to help meet the service needs of an institution, which leads to unsound practice; and payment of low stipends to foreign nurses, which tends to lower the economic status of American nurses.

Such practices, representing deviation from the original intent of the Exchange-Visitor Program, lead to serious consequences. This is especially true when the program is used as an employment instrument rather than an educational program.

The ANA is equally concerned with the recruitment of foreign nurses under immigration visas for the express purpose of their employment in the United States without adequate regard for licensing requirements or for their qualifications to carry out functions they are called on to perform. The ANA recognizes as acceptable practice the employment of graduate nurses who wish voluntarily to immigrate to the United States, provided they have adequate educational preparation for the functions they are expected to perform, are able to meet the licensing requirements for registration in a state, and possess a sufficient command of the English language to permit them to practice safely.

In view of the shortage of nursing personnel the world over, the ANA opposes the active recruiting, by advertisements or other inducements, of nurses from countries which are critically short of nurses. The ANA likewise condemns the practice of employing as subsidiary workers nurses who cannot meet licensing requirements. This practice is especially dangerous if such personnel are assigned responsibilities which should be restricted to qualified graduate nurses. Such employment practices not only run counter to accepted international professional concepts of good nursing education and practice but jeopardize the safe care of patients in the United States.

The American Nurses' Association, therefore, commends the purposes and objectives of the Exchange-Visitor Program and approves the legitimate employment of nurses in the United States under immigration visas, provided they meet requirements for licensure, but deplores abuses of the Exchange-Visitor Program leading to corruption of the original intent of the program and to unsafe nursing practice and the indiscriminate recruitment of nurses from other countries for the purpose of their employment as nurses in the United States.

Judith G. Whitaker, R.N.
Executive Secretary.

This statement is slightly abbreviated.

MEDICAL LITERATURE ABSTRACTS

INTERNAL MEDICINE

Effect of Thoracolumbar Sympathectomy on the Clinical Course of Primary (Essential) Hypertension: A Ten-Year Study of 100 Sympathectomized Patients Compared with Individually Matched, Symptomatically Treated Control Subjects. K. A. Evelyn, M. M. Singh, W. P. Chapman, and others. Am. J. Med. 28:188-221 (Feb.) 1960 [New York].

The first 50 men and the first 50 women with primary (essential) hypertension, on whom thoracolumbar sympathectomy was performed by Smithwick in the Massachusetts General Hospital between 1940 and 1945, were followed up by the authors for 10 years. Control data were obtained from the records of nearly 1,500 patients with essential hypertension who had received symptomatic therapy only and had been followed up in one of 3 cooperating hypertension clinics, (Massachusetts General Hospital, Boston, Columbia-Presbyterian Medical Center, New York, and Royal Victoria Hospital, Montreal) for a minimum of 10 years, or until death. The matching of propositi and control patients was "blind," on the basis of the initial findings only, so that each surgically treated patient was paired with a control patient, of the same sex and of closely similar age, who resembled the propositus with respect to the preoperative grades for each of the principal clinical and laboratory findings which reflect the course of hypertensive vascular disease in respect to blood pressure, cardiac, cerebral, renal, and retinal changes. Despite several admitted but unavoidable shortcomings, detailed comparison of the preoperative clinical findings in the 2 series did not indicate systematic bias in either direction.

A significant reduction in blood pressure was arbitrarily defined as a decrease of 2 or more grades in the average blood pressure measured under casual conditions, with the patient in the lying or sitting position. A lasting blood pressure reduction of this degree occurred in about 33% of the patients in the surgical series; but when those who died or had major complications despite the decrease in blood pressure were excluded, there remained only 10 men and 10 women whose blood pressure was significantly reduced, and who were alive and well at the end of 10 years. A similar favorable outcome occurred in only one patient in the control series. The operation was more effective in reducing the average level of blood pressure than in preventing the occurrence of occasional high values which, even in patients with the most clear-cut reduction of blood pressure grade, often reached levels almost as high as the highest recorded preoperatively. The average difference between the maximum preoperative and maximum postoperative blood pressures of the surgically treated patients was a decrease of 21 mm. Hg systolic and 15 mm. Hg diastolic, as compared with an increase of 7 mm. Hg in the systolic pressure and no change in the diastolic in the control patients. Orthostatic hypotension, which occurred in almost all the patients in the immediate postoperative period, was still present in about half of the survivors at the end of 2 years, the proportion being at least as high in those who were destined to die within the next 8 years as in those who survived the full 10-year period. Relatively slight degrees of orthostatic hypotension were still present in about 20% of the survivors at the end of 10 years.

Improvement of 2 or more grades in cardiac status did not occur in any patient in the control series, but at the end of 10 years cardiac symptoms had improved to this extent in 2 surgically treated patients, and electrocardiographic abnormalities had decreased by 2 grades in another. The incidence of unfavorable changes in cardiac status was lower in the surgical series than in the control series, the frequency of deterioration in cardiac symptoms, heart size, and electrocardiogram being 37, 4 and 14%, respectively, in the surgical series, and 43, 19, and 26% in the control series. Headache of moderate severity was significantly improved in 58% of the surgically treated patients, and in 41% of the control patients, but headache of grade 4 severity was seldom relieved, all 6 patients with headache of this intensity having died after an average interval of only 8 months. Cerebrovascular accidents occurred during the 10-year period in 62% of the surgically treated patients who had had a stroke before the operation, and in 28% of those who had not, the corresponding figures for the control series being 45 and 24% respectively. The incidence of deterioration in renal symptoms, proteinuria, and

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renal function was only 15, 5, and 26% in the surgically treated patients, as compared with 25, 18, and 36% in the control patients. Sympathectomy was significantly more effective than symptomatic management in bringing about the resolution of retinopathy and papilledema, as well as in reducing the frequency with which these complications occurred in patients who had been free of them at the start of the follow-up period.

The mortality rate at the end of 10 years was 41% in the surgical series (48% in men; 34% in women), and 47% in the control series (54% in men; 40% in women). A large fraction of the sex difference in mortality rate was due to the higher incidence of serious preoperative hypertensive complications. The clinical condition of those who survived the 10-year follow-up period was relatively satisfactory, the incidence of serious disability due to complications of the disease having been only 15% in each series. The results of this investigation confirm previous reports that thoracolumbar sympathectomy brings about favorable and occasionally dramatic changes in some of the clinical manifestations of hypertension in certain patients. However, as judged by the results of a direct comparison between surgically treated patients and individually matched control subjects, the over-all effect of the operation on morbidity and mortality in this small consecutive theories of cases was somewhat disappointing.

Quinidine in Chronic Atrial Fibrillation. I Freeman and J. Wexler. Am. J. M. Sc. 239:181-186 (Feb.) 1960 [Philadelphia].

The records of 100 consecutive patients, admitted to the Veterans Administration Hospital, Baltimore, between 1946 and 1952, with heart disease and atrial fibrillation of at least 2 weeks' duration, were reviewed. All had a history of cardiac decompensation or were decompensated upon admission, had evidences of valvular or myocardial disease, and were treated by bed rest, salt restriction, digitalization, and mercurial diuretics when necessary. Another series of 100 unselected patients, admitted between 1953 and 1958, were treated in the same manner with the addition of anticoagulants and quinidine. Bishydroxycoumarin (Dicumarol) was so administered that the prothrombin times ranged in the neighborhood of twice that of the untreated patients for a period of 12 to 14 days prior to the administration of quinidine. This was done in deference to those who believe that restoration to normal sinus rhythm increased embolization, and on the assumption that a 2-week period of anticoagulant therapy would prevent new thrombus formation and permit existing thrombi to organize. Quinidine sulfate was then administered in doses of 0.2 Gm. every 2 hours for 6 doses. An electrocardiogram was taken between the 4th and 5th doses. If the QRS duration was not increased by 25% or more, the remaining 2 doses of the series were administered. If severe nausea, vomiting, diarrhea, tinnitus, or prolongation of the QRS complex beyond 25% of that of the untreated patients occurred, the drug was withdrawn. If no untoward effects were noted, the schedule was repeated on the following days, with an increment of 0.2 Gm. of quinidine sulfate per dose per day until reversion was effected, toxic effects were evident, or a dose of 1 Gm. every 2 hours was reached. A maintenance dose of 0.2 to 0.4 Gm. of quinidine sulfate was given every 6 hours if reversion was accomplished. Dicumarol therapy was maintained for an additional 3 days after reversion.

Prolongation of the prothrombin time to twice that of the untreated patients was effected by Dicumarol administration over a period of 12 to 14 days prior to attempted reversion. Fifty-seven of the treated group reverted to normal sinus rhythm, and their conditions were so maintained on smaller doses of quinidine throughout the remainder of their respective periods of hospitalization. There was one death secondary to resistant decompensation and there were no embolic complications in the group receiving anticoagulants and quinidine, compared with 18 deaths and a 4% incidence of nonfatal thromboembolic complications in the untreated group. Ten patients who were still decompensated at the time of the attempted reversion, in spite of intensive therapy for 14 days, achieved compensation upon reversion and maintenance of normal sinus rhythm. Patients with bundle-branch block and marked cardiomegaly fared no worse than others. From these observations it appears safe and desirable to use vigorous measures directed toward establishing normal sinus rhythm on all hospitalized patients with chronic atrial fibrillation.

Variations in Serum Lipid Concentration and Clinical Coronary Disease. M. E. Groover Jr., J. A. Jernigan, and C. D. Martin. Am. J. M. Sc. 239:133-139 (Feb.) 1960 [Philadelphia].

An executive health program was begun at the instigation of the Surgeon General of the United States Air Force in the spring of 1950. The primary aim was a reduction in the incidence of clinical manifestations of coronary artery disease among the general officers and civilian executives at Air Force headquarters. Because of this primary aim, records were organized and laboratory studies were selected to add as much information as possible to the problem of atherosclerosis. Special emphasis was placed on a study of the cardiovascular system. In support of this study serum was examined for the determination of cholesterol, phospholipids, and lipoprotein fractionization by the ultracentrifuge and by a special study of electrophoretic patterns. Later, special studies were begun for the purpose of determining the cause of widely varying serum lipid levels. The laboratory studies were done at the time of the annual examination, and were repeated when the patients returned for any reason. The number of persons studied had reached 509 by Jan. 1, 1959.

One of the first points that was impressed upon the authors was the tremendous variation in serum cholesterol, phospholipids, and total lipoproteins. The variation was noted in all 3 laboratories doing cholesterol determinations and in both of the laboratories doing lipoprotein studies. To determine the relationship between clinical coronary artery disease and serum cholesterol concentration, 177 persons were selected, each having had 6 or more cholesterol determinations yearly for at least 5 years. Myocardial infarction developed in 16 patients in the group that showed the greatest variations in serum cholesterol. The variations were usually elevated considerably, 25% or more above the 5-year average. The variation in serum lipids seems to be more significant than the concentration in predicting the tendency to develop clinical evidence of coronary disease.

Is Mitral Stenosis More Severe in Men? G. Ricordeau, J. L. Chevrier, D. Dubost, and C. Dubost Presse méd. 69:55-57 (Jan. 16) 1960 (In French) [Paris].

The records of 124 men and of 124 women with mitral stenosis, on whom mitral commissurotomy had been performed by the same medical-surgical team between July, 1954, and July, 1957, were reviewed in order to compare the results and to judge whether mitral stenosis is more severe in men than in women. The records showed the patients' condition before, during, and after the operation, and indicated that mitral stenosis is more severe in men than in women. This fact was particularly noticeable, because operation has given good results less frequently in men than in women (70% in men, as compared with 83% in women), which was substantiated by fewer ultimate improvements in men (50% in men, as compared with 87% in women). There was a greater risk of aggravating the lesions during operation on men than on women (22 men, as compared with 10 women), and more men than women were, therefore, denied operation (15 men, as compared with 10 women). The occurrence of complications during the operation was also higher in men than in women (15 men, as compared with 8 women).

The particular severity of mitral stenosis in men seems to be due, on the one hand, to the higher incidence of atrial thrombosis (20.8% in men, as compared with 14% in women) and, on the other hand, especially to the anatomic structure of the mitral orifice itself, which renders commissurotomy in men more hazardous and difficult. The more frequent occurrence of a calcified mitral orifice associated with mitral insufficiency is one of the principal elements held responsible for the difference in the anatomic structure. Even when the factors causing the severity of mitral stenosis are more or less recognized before the operation, thus leading to a more cautious prognosis regarding the possibilities of surgical management, too conservative an attitude does not seem to be justified.

Tuberculosis of the Mouth and Throat: With Special Reference to the Incidence and Management Since the Introduction of Chemotherapy. T. A. Cawson. Brit. J. Dis. Chest 54:40-53 (Jan.) 1960 [London].

The author describes 4 cases of oral tuberculosis occurring in patients with pulmonary tuberculosis, 1 case of primary oral tuberculosis, 1 case of lupus vulgaris of the lip, and 8 cases of tuberculosis of the tonsils. Thirty-four cases of oral tuberculosis associated with pulmonary tuberculosis are reviewed. It is emphasized that the latter group is the most important, because this type of lesion is usually associated with advanced pulmonary disease. The tongue in these patients is the commonest site of the mucosal lesions, particularly the edge of the anterior part of the tongue. Ulceration is frequent, and in many patients fissures, granulomas, tuberculomas, and diffuse glossitis are present. Pain is usually severe, and extensive bilateral pulmonary lesions are usually present.

The most important aspects of this problem are to distinguish oral cancer from tuberculosis and to detect previously undiagnosed pulmonary tuberculosis. It is suggested that all but the most transient lesions of the mouth should be examined by biopsy, and there is no contraindication to this measure. A cytological examination of a smear from the lesion may give an immediate diagnosis. Patients with oral tuberculosis respond rapidly to chemotherapy, but the essential principles of treatment are that several antibiotics must be given to prevent the development of resistant strains of mycobacterium tuberculosis, and such chemotherapy must be prolonged to prevent a relapse. The prognosis of pulmonary tuberculosis today is good, and there is no reason to assume that the prognosis of patients with oral tuberculosis is inferior.

There are no characteristic clinical features of tuberculosis of the tonsils, and the diagnosis is only made after their removal and section. It seems, therefore, that surgical treatment of the lymph nodes will be unavoidable. Chemotherapy should be given to prevent hematogenous spread of the infection, especially in the younger child. Patients with primary oral tuberculosis, which seems to be prone to a high incidence of adenitis as a complication, and with lupus vulgaris should also be treated with combined chemotherapy for 2 years or longer. In patients with pulmonary tuberculosis complicated with dental infection, a biopsy exam-nation should be carried out to establish the specific nature of the infection. Prolonged systemic chemotherapy with several drugs is the treatment of choice for such patients.

Lycopenemia: A Variant of Carotenemia. P. Reich, H. Shwachman, and J. Craig. New England J. Med. 262:263-269 (Feb. 11) 1969 [Boston].

The authors present the history of a 61-year-old woman who was hospitalized because of recurrent pain in the right upper abdominal quadrant and apparent jaundice. Yellow color of the skin had been noticed 18 months before and had persisted. The patient's dietary history revealed an intake of 2 liters of tomato juice daily for several years. Because cholecystograms showed the presence of nonopaque stones, a cholecystectomy was performed; at the same time intestinal adhesions were lysed, and a liver biopsy specimen was taken. The liver was enlarged and was orange-yellow. The patient made an uneventful recovery, but after discharge she continued to have vague complaints in addition to pain in the right upper abdominal quadrant. Moreover, after a period of abstinence she had resumed her heavy intake of tomato juice.

The finding of a normal bilirubin value in the presence of the yellow skin and the admission diagnosis of obstructive jaundice led to consideration of other possible causes of the discoloration. The blood carotenoid level was found to be 113 units per 100 ml., a value high in the carotenemia range, since the normal range is 30 to 60 units. Tomato juice contains large amounts of lycopene, a physiologically inert structural isomer of beta-carotene. Lycopene and beta-carotene have absorption maxima of 475 and 452 A units, respectively, so that the colorimetric test would not distinguish between them. A petroleum-ether extract of the patient's favorite brand of tomato juice gave an absorption curve comparable to that of her serum. The possibility that the pigment disorder was due to an excess of lycopene rather than beta-carotene was investigated.

A normal young man was given 1 liter of tomato juice to drink, and his carotenoid level, as measured by colorimetry, rose 34 units per 100 ml. above the fasting level in 45 minutes and then fell to the fasting level in 90 minutes. When the patient was given 1 liter of tomato juice, her serum showed an increase of 20 units per 100 ml. above the original carotenoid level, with a fall to its usual high value after 2 hours. Over a 3-week period, on a diet free of tomato juice, the patient's skin color faded, and the serum colorimetric readings fell from a high of 117 to 92 units per 100 ml. The woman's condition was distinguished from common carotenemia by the source of the carotenoids, the color of the skin, the specific carotenoids involved, and their storage in the liver.

SURGERY

Primary Repair of Compound Skull Fractures in Children. K. W. Carrington, J. A. Taren, and E. A. Kahn. Surg. Gynec. & Obst. 110:203-209 (Feb.) 1960 [Chicago].

While almost all neurosurgeons agree with the principle of early débridement of compound skull fractures, there are many differences of opinion as to the immediate handling of the bony defect which follows débridement. During a 7-year period at the University of Michigan Hospital, Ann Arbor, 20 children with compound skull fractures have been treated by replacing the free bone fragments as a primary procedure in 19 and by a primary acrylic cranioplasty in 1. In all but 2 of the children débridement, with replacement of the bone fragments, was carried out within 2 or 3 days of the accident. All these patients have been carefully checked postoperatively, and primary healing without pulsatile defect at the site of repair has resulted in all instances. There have been no complications. Fourteen patients had dural lacerations which were closed primarily or with dural grafts, and 12 patients had cortical lacerations with loss of brain tissue. In no case, however, has a permanent neurological deficit resulted. Even in the absence of dural lacerations, it is advised that a small opening be made in the dura at the time of the primary repair to permit subdural exploration.

Three patients had convlusions in the immediate postoperative period, but these are generally focal in type and do not necessarily recur, nor do they carry the serious import of those which occur subsequently. Twelve of the children who had brain lacerations have been traced for from 7 months to 9 years. Since there have been no convulsions in any of these patients, it seems that the incidence of post-traumatic epilepsy may have been reduced in this series. The authors stress the necessity of dural closure, either primarily or by graft, if the bone fragments are to be replaced. The supraorbital ridge has twice been replaced as a free fragment, with an excellent cosmetic result.

Treatment of Chronic Coronary Insufficiency: Ligation of Internal Mammary Arteries in the Second Intercostal Space. A. N. Bakulev and Kh. N. Muratova. Klin. med. 38:41-48 (Jan.) 1960 (In Russian) [Moscow].

Bilateral ligation of internal mammary arteries in the 2nd intercostal space was performed on 60 patients above 30 years of age, with chronic coronary insufficiency, at the institute of chest surgery of the Academy of Medical Sciences of the U. S. S. R. during the past 2 years. Three patients died within 4 days after the operation. Satisfactory results were observed immediately after the operation in 54 patients and on discharge in 42. Electrocardiographic findings could not demonstrate improvement in the immediate postoperative period despite the subjective feeling of improvement of the patients. Long-term results were satisfactory in 39 patients and unsatisfactory in the others. Pain reappeared in some patients within 3 months after the operation. Improved coronary blood flow was shown in patients with excellent and good postoperative results on electrocardiographic examination made within several months after the operation.

This study indicates that immediate and late postoperative results of bilateral ligation of internal mammary arteries for the treatment of chronic coronary insufficiency are good. The authors recommend this operative procedure in view of the satisfactory postoperative results and the relatively minor trauma involved.

Attempts at Surgical Treatment in Acute Myocardial Infarction. A. N. Bakulev and V. V. Lebedev. Klin. med. 38:48-55 (Jan.) 1960 (In Russian) [Moscow].

Twenty patients with acute myocardial infarction and 10 with a preinfarction condition were operated on by ligation of internal thoracic arteries at the institute of chest surgery of the Academy of Medical Sciences of the U. S. S. R. in 1959. Most of the patients were between 51 and 57 years old. Operation was performed on 10 patients within the first 2 days and on the others from 3 to 24 days after the onset of myocardial infarction. There were 2 operative deaths. Total infarction of the walls of the left ventricle was revealed in both patients at autopsy. On discharge excellent results were observed in 8 patients, good in 17, and fair in 3. The general condition of the patients improved during the 1st postoperative day. Weakness and sweating disappeared, and pain in the region of the heart either decreased or disappeared.

The authors recommend that surgical treatment of myocardial infarction should be undertaken as soon as the first symptoms of the disease appear. Surgical treatment will have a long-term effect only if adequate anastomosis of blood vessels between the myocardial and extracardial vessels takes place.

Results of Shunt Procedures in Tetralogy of Fallot. H. B. Shumacker Jr., and I. Mandelbaum. Surgery 47:320-327 (Feb.) 1960 [St. Louis].

One hundred six patients with the tetralogy of Fallot were treated primarily by systemic-pulmonary artery anastomosis. There were 55 female and 51 male patients, ranging in age from 2 months to 27 years. No patient under the age of 18 months was operated on unless the clinical course was so poor as to make the operation mandatory. Eighty-six subclavian-pulmonary artery shunts and 29 aortic-pulmonary artery anastomoses were performed. Ninety-five patients underwent a single shunt procedure, and 11 required reoperation. Five of the patients subjected to a shunt procedure died during the operation or during the postoperative period. Only 2 deaths occurred among the 77 patients who were older than 18 months. Six deaths occurred later, all of them in the 18-month-old or younger group. Several minor complications occurred during the postoperative period. Three patients had a transient Horner's syndrome; 2 required temporary underwater seal drainage for postoperative pneumothorax; and 1 developed a chylothorax which required thoracotomy and ligation of the thoracic duct. One 16-month-old girl developed acute pulmonary edema after a Potts anastomosis. Other complications occurred late from 6 to 8 years after the operation. Three patients developed subacute bacterial endocarditis and 1 had cerebral thrombosis and right-sided hemiplegia.

The postoperative status of the patients was considered good when there was decrease in cyanosis together with subjective improvement and increased exercise tolerance. It was considered fair when there was some subjective improvement, whereas cyanosis and below-normal exercise tolerance persisted. Eighty-nine patients were followed up for periods varying from 2 to 10 years. Fifty of the 63 living patients who were 18 months old or older at the time of the operation obtained good results; 9 had fair results; and 3 remained unimproved. Fourteen of 19 living patients who were under 18 months at the time of the operation had good results; 3 had fair results; and 1 was unimproved. Continued use of the shunt procedures will probably bring improvements, and one may anticipate a mortality in the range of 1%. A more aggressive attitude toward reoperation, in case the operative shunt proves to be too large or too small, might increase the percentage of patients with ultimately good results.

Defect of the Atrial Septum in the Elderly: Report of Successful Surgical Correction in Five Patients Sixty Years of Age or Older. F. H. Ellis Jr., R. O. Brandenburg, and H. J. C. Swan. New England J. Med. 262:219-224 (Feb. 4) 1960 [Boston].

Four women, between the ages of 60 and 64 years, and a 61-year-old man were operated on for defects of the atrial septum. Significant cardiac symptoms had been present for 8 years before surgical intervention in 3 patients, for 7 years in 1, and for 2 months in 1. Murmurs had been heard many years previously in 3 of the 5 patients. Symptoms progressed rapidly; at the time of the operation 3 of the patients were placed in class 4 (most severe), 1 in class 3, and 1 in class 2, according to the classification of the New York Heart Association. All the patients showed typical clinical features. The heart was enlarged and overactive, with an "ejection length" systolic murmur, heard best in the 2nd and

3rd left intercostal spaces. A systolic thrill was also present in 2 patients. The pulmonic 2nd sound was split throughout the respiratory cycle. There was also clinical evidence of failure of the right heart, characterized by venous distention and enlargement of the liver, in 4 of the 5 patients. Chest roentgenograms showed cardiac enlargement, with prominence of the pulmonary-artery segment and increased pulmonary vascular markings. The electrocardiograms showed the configuration of partial or complete right bundle-branch block. Four of the 5 patients had atrial fibrillation. All the patients had increased pulmonary-artery pressure, but only one had a hemodynamically significant right-to-left shunt.

Because of the low operative risk and the excellent results accompanying closure of septal defects by means of the atrial-well technique of Gross, this method was employed in 2 of the 5 patients. Extracorporeal circulation was employed in the other 3 patients because of severe failure of the right heart, with an increased pressure in the right atrium that precluded use of the atrial well. The defects in 4 of the 5 patients were small in comparison with those found in younger patients; these 4 defects measured from 1.8 to 5 cm. in diameter. The use of a prosthesis fashioned from Teflon or noncompressed Ivalon is advisable, even though the defects in these older patients are relatively small.

All patients survived the operation and have symptomatically improved. One patient still appears to be slightly disabled. Three of the patients have been reexamined at the clinic 4 months, 1 year, and 3 years after operation respectively. Unequivocal reduction in the size of the heart has occurred in 2 patients whose chest roentgenograms were available for comparison. The reported data clearly indicate that, in the presence of significant symptoms and a large pulmonary blood flow, surgical correction is indicated and can be accomplished successfully, at low risk in patients over 60 years of age, and with gratifying results.

Late Observation of Bronchus Stump After Pneumonectomy for Lung Cancer. V. A. Mikhalchenko. Probl. Onc. 4:607-613 (no. 5) 1958 [New York].

Sixty patients who had undergone pneumonectomy for lung cancer were given clinical x-ray examination with special methods for the study of postoperative bronchus stump. The interval between the operation and the examination varied between 1 month and 6 years. Thirty-one patients were living and in good health at the time this article was written; 9 of them had been operated on from 3 to 5 years previously. Of the 29 patients who survived less than 2 years, 18 died of metastases in remote organs; 8 died of degeneration of the bronchus stump and subsequent empyema of the pleura, due to the intergrowth of metastases. By means of a combination of stump bronchography and kymography, it was established that the bronchus stump in uncomplicated cases makes definite oscillatory motions in which its extension with inspiration and concentric contraction with expiration are visible. The form of the bronchus stump after pneumonectomy depends essentially on the method by which it was treated, although it is also conditioned by the formation of ligature granulations, fistulas, cancerous recurrences, and compression of the bronchial stump by enlarged mediastinal lymph nodes as a result of metastases within them. Cancer recurrence in a bronchus stump was observed only once in the clinical and x-ray examinations.

Histological examinations on the 60 patients showed that only in 23 had the bronchus been intersected within the limits of healthy tissue. Eight of these patients had metastases in deep-seated lymph nodes and died within 2 years after the operation. The bronchus was cut away within the limits of cancerous infiltration in 8 patients. Six of these died within 2 years of generalized metastases. Inflammatory changes were found in 29 patients. These late observations indicate that the recurrence of a cancerous tumor in the stump is infrequent even when cancerous cells are discovered at the margin of the section. A distinction must be made between the true recurrence of a tumor in the bronchus stump which develops in the wall itself and a secondary disease caused by a tumor which in time spreads from metastatically affected mediastinal lymph nodes.

A 5-Year Follow-Up Roentgenologically Detected Lung Cancer Suspects. L. W. Guiss. Cancer 13:82-90 (Jan.-Feb.) 1960 [Philadelphia].

During 1950 chest minifilms were taken of a total of 1,867,201 persons, or almost 60% of the Los Angeles County population over 15 years of age. Although the chief purpose of this survey was the detection of tuberculosis, 3,500 lung tumor suspects were found; these were incorporated into a tumor registry and have been followed up to determine what might be the natural history of such a group. In 1955 a paper was published summarizing the experience of this closed group during the first 3 years after the survey, together with certain conclusions about the effectiveness of roentgenographic screening as a lung cancer control measure. This current and final report reviews the status of the same group at the end of 5 years or more from the time of minifilming. A rather large segment of the original 3,500 patients (620, or almost 18%) were lost to follow-up, and 748 (21%) were known to be dead at the end of 5 years.

The incidence of, and death rate from, bronchogenic carcinoma appears to increase annually. The salvage from this disease by surgical treatment has not improved during the past 10 years, largely because of relatively late diagnosis and treatment and, to a lesser degree, because of limitations inherent in current surgical techniques. Any improvement in cure rates for lung cancer will stem, not from extensions of scope of surgical treatment, but rather from earlier treatment of curable cases. Periodic repetitive roentgenography of the chest is currently the only generally available and practical method of detecting lung cancer before it becomes symptomatic or incurable. If pulmonary screening programs are restricted to selected groups and to men over 45 years of age, the yield in lung cancer cases may be increased immensely.

The group of chest neoplasm suspects identified in a single survery continues to yield a high incidence of lung cancer several years after the survey. Much of the potential improvement in cure rate for lung cancer among those identified as being tumor suspects is lost through dilatory medical management and patient reluctance to submit to investigation. The size of the pulmonary lesion, provided that it is surgically resectable, has no definite correlation with either symptomatology or prognosis in this material. The asymptomatic patient has 3 times the chance of cure as has the patient with clinical signs before surgery. If facilities for differential diagnosis are not at hand to permit prompt evaluation of suspects, or if those so identified are not willing to cooperate in this evaluation and submit to treatment, there would seem to be no purpose in any such roentgenographic screening program.

Superior Mesenteric Artery Syndrome. G. C. Kaiser, J. M. McKain, and H. B. Shumacker Jr. Surg. Gynec. & Obst. 110:133-140 (Feb.) 1960 [Chicago].

Superior mesenteric artery syndrome is an unusual form of high intestinal obstruction. The authors present their observations on 18 patients who received surgical treatment for this condition at the University Medical Center and the associated Veterans Administration Hospital in Indianapolis during the past 6 years. The patients ranged in age from 8 to 81 years, but most were young adults. In 7 patients the disorder was acute; in 11 it was subacute or chronic. The acute form occurs without a previous history of gastrointestinal symptoms and is usually precipitated by a somewhat prolonged period of immobilization necessitated by unrelated disease, injury, or operation. It is especially likely to occur when patients are forced to lie supine; they become nauseated, complain of abdominal distress and distention, and vomit. The subacute or chronic form tends to occur in tall, slender, or undernourished types of people. They complain periodically of flatulence, postprandial epigastric fulness, and vomiting of bile-stained material usually containing recently eaten food. Some obtain relief by lying prone or assuming the knee-chest position. When examination is carried out on patients whose stomachs have not been decompressed by emesis or nasogastric suction, gastric distention may be evident.

The diagnosis can often be suspected from plain roentgenograms of the abdomen which may show gaseous distention of the stomach and duodenum with little or no gas beyond the point of obstruction. Roentgenograms are of less help when the stomach is distended with fluid alone, or when the stomach and duodenum have been emptied by aspiration or vomiting. The diagnosis can almost always be established by roentgenologic study with a contrast medium. The stomach and duodenum are large; the pylorus is patulous. The obstruction is seen as a more or less straight-line shutoff of the duodenum along the lateral border of the psoas shadow on the right. By fluoroscopy, reverse persistalsis and churning of duodenal contents may be noted. Cholecystography may indirectly lead one to suspect some type of duodenal obstruction if the dye opacifies the stomach and duodenum, or if the gallbladder reopacifies over a period of days.

Medical management may be successful, especially in acute cases. Nasogastric suction should be instituted and fluids given intravenously to maintain water and electrolyte balance. If the patient has been bedridden, he should be made ambulant if this is feasible. If not, placing him in the left lateral or the prone position may be helpful. When medical management fails, surgical intervention is indicated. A number of surgical methods have been recommended, but the authors are convinced that duodenojejunostomy is the best treatment, not only for the superior mesenteric artery syndrome but also for duodenal atresia, duodenal stenosis, and annular pancreas. This anastomosis can easily be performed under local anesthesia, which may be advantageous in a critically ill patient. Recently it has been suggested that division of the ligament of Treitz and freeing the distal portion of the duodenum may bring about relief of symptoms. The authors feel that this proposal deserves further trial, but if obstruction cannot be adequately relieved in this fashion, it should be bypassed by duodenojejunostomy.

Study of Esophageal Cancers of Unusual Onset. P. Hillemand and J. Leymarios. Semaine hôp. Paris 36:150-155 (Jan. 18) 1960 (In French) [Paris].

The authors report on 5 patients with atypical initial forms of esophageal cancer. The first patient, a 64-year-old man, had a sudden acute attack of dysphagia which disappeared spontaneously within 3 or 4 days. Roentgenologic and esophagoscopic findings were negative for cancer and indicative of an epiphrenic diverticulum. The dysphagia recurred 4 months later, and new roentgenograms showed an image suggestive of cancer. A cinematographic study confirmed the diagnosis. The patient was treated surgically and was in good health 2 years after the operation. In the other 4 patients reported, the first symptom was hemorrhage. In 3 patients there was no dysphagia before the 1st hematemesis, and in 1 there was a slight and recent dysphagia. The authors stress the need for a thorough examination of the esophagus in any patient with hematemesis of unknown etiology.

Pheochromocytoma in Children: Case Report and Discussion of the Use of Adrenolytic Agents in Conjunction with Operation. H. A. Zintel, J. F. Eagle, P. Skok, and S. Arnaud. Surgery 47:328-339 (Feb.) 1960 [St. Louis].

An 11-year-old boy was hospitalized on a tentative diagnosis of functioning pheochromocytoma, after suffering from periodic frontal headaches, blurred vision, vomiting, and hypertension for 2 years. The patient's blood pressure was 230/185 mm. Hg; a 24-hour urine specimen contained 2,400 mcg. of catecholamines; a blood specimen, obtained on the same day, showed a concentration of 30 mcg. of catecholamines per liter of plasma. In an attempt to localize the tumor, 340 cc. of oxygen was injected in the presacral area, and simultaneous intravenous pyelograms were obtained. In addition, right and left oblique films and tomograms were taken. A round mass was shown in the area of the right adrenal gland, displacing the superior major calyx of the right kidney.

An attempt to prepare the patient for operation was made with phentolamine given orally. It failed to maintain a satisfactory lowering of the blood pressure, and was abandoned because of marked diaphoresis and tachycardia. Preoperative medication consisted of 50 mg. of pentobarbital given orally and 0.3 mg. of scopolamine injected subcutaneously 2 hours before the operation. The right adrenal gland containing the tumor was removed, and the right flank incision closed in a one-hour operation. The blood pressure fell to 108/62. The patient received 200 cc. of whole blood and an infusion of arterenol, 8 mcg. per cubic centimeter in 5% dextrose in water, at the rate of 50 drops per minute. This treatment was discontinued after a period of 7 hours. One week after the operation a 24-hour catecholamine determination was reported to be 150 mcg., still twice the normal value.

Since the high blood pressure persisted after the patient was discharged, he was hospitalized again 7 months after the operation, and a left adrenalectomy was performed. The blood pressure reached a low point of 100/60 at the time of removal of the tumor. The patient received 500 cc. of whole blood, and an infusion of 8 mcg. of arterenol in 500 cc. of 5% dextrose was started. After 2 intravenous injections of 25 mg. of hydrocortisone sodium succinate (Solu-Cortef), the patient's blood pressure appeared to stabilize at 140/80. On the 3rd postoperative day the parenteral cortisone medication was changed to oral doses of 25 mg. every 12 hours. One week postoperatively the administration of 0.1 mg. of 9-alpha-fluorohydrocortisone was added. The patient was discharged one month after the second operation, still on the cortisone and 9-alpha-fluorohydrocortisone treatment.

The authors point out that, although a prophylactic treatment with adrenolytic agents is apparently beneficial in patients with pheochromocytomas, it may cause the development of multiple tumors. Reports on 13 patients with solitary tumors, operated on without the prophylactic use of adrenolytic agents, record good results with no mortality.

New Possibilities of Surgical Decompression in Animals with Portal Hypertension Due to Intrahepatic Obstacle. F. Cataliotti, L. Li Castri Patti, and G. Di Pace. Minerva chir. 14:1457-1468 (Dec. 15) 1959 (In Italian) [Turin, Italy].

New surgical techniques for the decompression of portal hypertension were tried in a series of 90 rats divided into 4 groups. The 1st group, composed of 30 animals, was used as a control group, being divided into 3 subgroups of 10 each. Portal hypertension was induced by ligation of the vena porta in the hepatic hilus in the 1st subgroup, by progressive and gradual stenosis of the subhepatic portal trunk in the 2nd subgroup, and by hepatic fibrosis resulting from induced chronic intoxication by daily exposure for 90 days to carbon tetrachloride in the 3rd subgroup. The other 3 groups of 20 animals each were divided into subgroups of 5 animals. Gastrohepatopexy, splenohepatopexy, splenonephropexy, or enteronephropexy was performed on the animals of each of these subgroups. In these 3 groups portal hypertension was induced by ligation of the vena porta in the hepatic hilus 60 days after the performance of the various operations in the 1st group, by gradual and progressive stenosis of the subhepatic portal trunk in the 2nd group, and by hepatic fibrosis induced by inhalation of carbon tetrachloride in the 3rd group. The results of the study show that the various surgical techniques employed had a decompressive effect on the portal system. It is pointed out that in methods in which the liver is used as the efferent organ of the caval circulation the decompressive technique is conditioned by the drainage deriving from the capsular and subcapsular vessels.

The authors believe that further study in this field is necessary, since surgical techniques, such as those employed in this study, may have a decompressive effect, even in cirrhosis, without depriving the liver of the portal flow. At the same time, especially on the basis of new concepts concerning the hepatogenous nature of ascites, there may be some indications for elimination of this phenomenon by means of the new anastomosis that results from pexis of the lymphatic regions of the 2 organs which are brought into contact.

Local Treatment of Burns. V. Bergonzelli and A. Fontana; Minerva chir. 14:1535-1542 (Dec. 31) 1959 (In Italian) [Turin, Italy].

The authors report on their experience with the local treatment of burns in a series of patients observed at the clinic for general surgery of the University of Turin. They conclude that the "open air method" is the most satisfactory one for the local treatment of 1st-degree, 2nd-degree, and 3rd-degree burns. The authors give first the most appropriate treatment for combating pain, shock, infection, and hemodynamic, protein, or electrolytic imbalances. The patient who has suffered burns is considered as suffering from multiple lesions, each differing from the others in pathogenesis, pathological structure, prognosis, therapeutic indication, and reparative capacity. In cases of local septic complications the crust is removed, and wet therapy, by means of packs containing an antiseptic solution of the Dakin type, is applied.

The proper treatment of 3rd-degree and 4th-degree burns consists in an early excision of the eschar, followed by grafting. When early excision is not possible because the patient is in a state of shock, surgical decompression by means of deep incisions in the devitalized areas is advised. In a case of severe trauma and collapse, it is advisable to perform excision of the eschar and to rehabilitate the patient by the method most suitable in his case. Bleeding areas are covered with skin grafts applied as early as possible, with autoplastic material. It is suggested that the application of homoplastic skin be reserved for very rare cases, especially when the patient is in a grave condition.

NEUROLOGY & PSYCHIATRY

B_{12} Metabolism and Multiple Sclerosis. J. S. O'Connor, R. L. Davis, O. R. Langworthy, and B. F. Chow. Proc. Soc. Exper. Biol. & Med. 103:180-183 (Jan.) 1960 [Utica, N. Y.].

Because of the beneficial effect of vitamin B_{12} in preventing and even reversing the demyelinizing effects of pernicious anemia, it has been assumed that vitamin B_{12} also plays a role in multiple sclerosis, and the effects of the administration of B_{12} in patients with multiple sclerosis has been investigated in a number of clinics with variable results. This paper is concerned with studies that were carried out to ascertain: (1) whether there are biochemical signs of B_{12} deficiency in subjects with multiple sclerosis by measuring B_{12} serum levels and glutathione (GSH) contents in the erythrocytes, and (2) whether such patients can metabolize orally or parenterally administered vitamin B_{12} as do clinically healthy subjects.

It was found that, as a group, patients with multiple sclerosis do not metabolize vitamin B_{12} and GSH in the same quantitative manner as does a contratest group. Their average vitamin B_{12} serum level is lower, as is their ability to retain the vitamin when administered intramuscularly, although they absorb adequately. Average GSH content of the red blood cells was reduced in the group of patients with multiple sclerosis. When a vitamin B_{12} tannate derivative was administered to such patients, vitamin B_{12} was excreted much more slowly in the urine than was aqueous vitamin B_{12}.

Acute Bronchial Asthma: I. Concomitant Depression and Excitement, and Varied Antecedent Patterns in 406 Attacks. P. H. Knapp and S. J. Nemetz. Psychosom. Med. 22:42-56 (Jan.-Feb.) 1960 [New York].

From the pathophysiological point of view, it is generally conceded that the primary pulmonary feature in asthmatic breathing is obstruction within the smallest air passages. Bronchospasm, pulmonary edema, and hypersecretion all lead to obstruction, but it is not certain which is primary. They all may follow exposure to histamine. The introduction of an allergen can lead to local release of histamine-like substances. Stimulation of the parasympathetic nervous system releases similar substances and may play a significant role. In the emotional sphere the precise sequence of events, before and during asthma, is equally in need of elucidation. To this end the authors have reviewed, clinically and retrospectively, 406 acute asthmatic attacks, described in the records of a study which included more than 50 cases of bronchial asthma. From the larger series, 9 patients were selected who had severe perennial asthma and who had been studied by at least 75 interviews, in psychotherapy or, in 2 cases, by psychoanalysis. Information was sought about concomitant feelings and fantasies accompanying attacks, and about antecedent events occurring in the 48-hour period prior to onset.

Feelings and fantasies concomitant with asthma tended to be dominated by absorption in the physical illness. At times this appeared to serve as a protection against obvious psychological problems. In somewhat more than half of the episodes other emotional concomitants appeared after asthma had become established. The vast majority of these were depressive—a sense of sadness, helplessness, and hopelessness, at times accompanied by ideas of a dangerous or poisonous inner substance. In contrast to them in somewhat less than half of the attacks, there were prodromal emotional manifestations which preceded and led directly to acute asthma. The principal prodromal feature was excitement, usually with an angry or anxious coloring, occasionally elated and erotic, resembling a miniature hypomania. The authors suggest that in asthma an initial phase of drive-arousal and excitement is followed by a later phase of drive-restraint and inhibition.

Antecedent changes in the environment occurring in the 48 hours prior to an attack varied widely. Eight categories could be discerned. Most of the categories could be divided into 1 of 2 groups: events which seemed to lead to frustration of powerful impulses, and those which seemed to stimulate erotized or dangerous wishes. The authors postulate that both types of event, although neither is of itself specific for asthma, might activate a respiratory apparatus having both intake and expulsion functions, which has become vulnerable to psychological as well as physiological stress.

Myopathies and Epilepsy: Clinical and Experimental Study. J. J. B. Goyanes, J. L. B. Salorio, and D. B. Salorio. Rev. españ. oto-neuro-oftal. 18:295-305 (Sept.-Oct.) 1959 (In Spanish) [Valencia, Spain].

The authors report on the coexistence of epilepsy with 3 types of myopathy—progressive muscular dystrophy, congenital amyotonia (Oppenheim's disease), and myasthenia gravis. They found epilepsy in 5 of 84 patients with progressive muscular dystrophy, in 2 of 7 patients with Oppenheim's disease, and in 1 of 18 patients with myasthenia gravis. These findings indicate that epilepsy is not an accidental development in the course of certain myopathies, and that there is a physiopathological relationship between these conditions. The muscular plaque in the myopathic patient needs a greater concentration of acetylcholine, a substance which is supposedly responsible for the epileptic attack. A predisposition to epilepsy develops as the patient's system, in a defensive mechanism against the myopathic blocking, increases the amount of acetylcholine in an effort to adjust to and overcome the disease. This hypothesis led the authors to an experimental study.

Eight male rabbits, weighing from 1.5 to 3.0 kg., received a subconvulsive dose of pentylenetetrazol (Metrazol)—0.75 mg. per kilogram of body weight. The effects of this drug were then investigated by means of electrocorticograms, electrocardiograms, and electromyograms. There were slight alterations in the electrocorticograms with either decrease or increase in voltage, sometimes with higher frequency, sometimes with isolated spikes. No changes were found in the electrocardiograms. In the electromyograms some discharges coincided with myoclonic contractions. One hour after the electrocorticograms had become normal, minimal doses of curare (0.66 mg. per kilogram of body weight) were injected intravenously. Control animals had only a slight hypotonia with alterations in breathing. In the experimental animals, 3 seconds after the injection of curare all electrocorticograms showed a marked and generalized change, with slow irregular waves and an increasing number of spikes. There were typical attacks in 50% of the animals, with synchronic generalized peak-waves of low voltage. The fact that the attacks had a centrencephalic origin with little involvement of the cortex led the authors to a new conclusion about the relationship between myopathy and epilepsy. In order to contract, the muscle must be prepared and must have a certain degree of tonus. The injection of curare alters this muscular tonus causing hypotonia. The afferent system of myofibrils increases its activity to overcome the hypotonia, which produces a predisposition in the centroencephalon; the injection of Metrazol in doses innocous to the rest of the nervous system brings about centrencephalic discharges. This seems to be the mechanism which operates in patients with myopathies with a marked hypotonic element, such as progressive muscular dystrophy, congenital amyotonia, and myasthenia gravis. In these patients the frequency of epilepsy is much higher than in the normal population. On the other hand, in hypertonic diseases, such as paralysis agitans (Parkinsons disease), the incidence of epilepsy is much lower.

Intermittent Carotid and Vertebral-Basilar Insufficiency Associated with Polycythemia. C. H. Millikan, R. G. Siekert, and J. P. Whisnant. Neurology 10:188-196 (Feb.) 1960 [Minneapolis].

The authors report on 22 patients with intermittent cerebral vascular insufficiency associated with polycythemia, who were observed at the Mayo Clinic between 1954 and 1957. The cases of 10 of these patients (7 men, between the ages of 43 and 73 years, and 3 women, between the ages of 43 and 65 years) are described in detail. All the patients had polycythemia vera, secondary polycythemia, or relative polycythemia. The clinical phenomena which were observed in these patients were essentially the same as those seen when polycythemia or focal cerebrovascular insufficiency occurs singly. In 8 of the 10 patients the presenting complaints were the episodic symptoms characteristic of attacks of cerebrovascular insufficiency. Such phenomena as plethora of the lips, cheeks, fingers, and toes, engorgement of the retinal veins, and increased size of the spleen may lead the clinician to suspect the presence of polycythemia.

These signs, however, can be minimal or absent. One patient with repeated sudden attacks of vertigo, nausea, vomiting, and impairment of vision, in whom a clinical diagnosis of intermittent insufficiency of the vertebral-basilar system, pulmonary arteriovenous fistula in the right upper lobe, and secondary polycythemia was made, had the pulmonary arteriovenous fistula surgically removed and had no further attacks of vertebral-basilar insufficiency. In 2 patients the polycythemia was quickly controlled, and effective control was maintained. One of these patients was well for 7 years after the control was established; then came 2 warning attacks of carotid insufficiency, followed 4 days later by permanent hemiplegia that began when the hematocrit was high. The other patient was well for 15 years after his polycythemia vera was controlled; then came warning attacks and, before the polycythemia vera was controlled again, cerebral thrombosis caused permanent damage to the brain.

These observations emphasize the fact that the initial important phenomenon occurring in a patient with polycythemia can be an attack of insufficiency in the carotid or the vertebral-basilar system; that it is necessary to examine the blood for polycythemia in every patient with focal cerebrovascular insufficiency; that the type of polycythemia should be determined, as specific therapy may be indicated, such as surgical intervention in the patient with arteriovenous fistula; that, when focal cerebrovascular insufficiency occurs in patients known to have polycythemia, the latter should be controlled as rapidly as possible, and that it may be necessary to administer anticoagulants for a variable period, depending on the frequency and severity of the attacks of focal cerebrovascular insufficiency.

Various concepts of the pathogenesis of intermittent insufficiency in the carotid and vertebral-basilar systems, such as transitory constriction of cerebral blood vessels (vasospasm), transient systemic hypotension, and temporary occlusion of a brain vessel by tiny emboli from a distance source, have been proposed by other workers. In the authors' patients it appears likely that there is at least some partial cause-and-effect relationship between the polycythemia and intermittent cerebrovascular insufficiency. The association of intermittent cerebrovascular insufficiency and polycythemia appears to supply one more bit of evidence implicating some part of the mechanism of thrombosis in the pathogenesis of the attacks of insufficiency.

PEDIATRICS

Electroencephalogram of the Infant Born in Normal and in Dystocic Labor. F. Cattaneo, C. Villavicencio, and N. Chiofalo S. Rev. chilena pediat. 30:303-307 (Nov.-Dec.) 1959 (In Spanish) [Santiago, Chile].

One hundred one newborn infants (71 born in normal labor and 30 in dystocic labor) received electroencephalographic examinations with monopolar and bipolar leads. Intermittent sound and light stimuli were used, with frequencies that varied between 6 and 15 flashes a second. The infants were also examined neurologically, with special emphasis on motility, peripheral sensitivity, and basic reflexes of suction and prehension. The electroencephalographic records were then compared as to the infants' age, duration of the dilatation and expulsion periods in labor, drugs administered to the mother, type of delivery, and kind of anesthesia.

The 2 groups, infants born in eutocic labor and infants born in dystocic labor, presented similar electroencephalographic features in most respects; the differences were observed in connection with the drugs administered to the mother and the kind of anesthesia. Meperidine hydrochloride, (Demerol) the only drug administered to the mothers who had an eutocic labor, was correlated with median and low voltages and with high frequencies. Spinal anesthesia and anesthesia induced with a chloroform-ether mixture were correlated with median and low frequencies. While the effects of both the drugs and the kind of anesthesia on the infants' response to light and sound were being analyzed, it was observed that one group did not respond to any of these stimuli. The only correlation found for this lack of response was the use of chloroform-ether in inducing anesthesia in the mother.

Hypothyroidism: Review of 19 Cases. O. Alonso, E. Mundt, and R. Gonzalez. Rev. chilena pediat. 30:314-317 (Nov.-Dec.) 1959 (In Spanish) [Santiago, Chile].

The authors report on 19 patients (12 females and 7 males), ranging in age from 1 to 23 years, whose hypothyroidism was evident in childhood. The diagnosis had been established after the age of 2 years for most patients; only in 5 had it been made earlier. The interval between the onset of the disease and the start of the treatment varied from 2 to 16 years. The authors believe that the length of this interval played an important part in the results of the therapy given to the 19 patients, and that the early onset of the disease suggests a congenital etiological factor. The patients had disproportionate body measurements and were from 59 to 93% smaller in size than the average person of their respective ages. Comparatively large cranium, short extremities, overweight, cretinoid facies, myxedematous infiltration of the skin, diaphoresis, dry and rough skin were general features in this series. The so-called sluggish vital tonus syndrome, characterized by mental retardation, cold-bloodedness, slow speech, anorexia, constipation, and slow pulse, was present in the 19 patients. Epiphysial dysgenesis was observed in 5 patients and involved different centers of ossification.

The treatment consisted of the administration of thyroid extract in doses which varied from 10 to 30 units for the younger children, and were larger for the older patients. Favorable results were noted in 15 patients who were followed up for periods of

11 months to 9 years. The first symptoms to abate were those of sluggish vital tonus. There was a rapid static-dynamic corporal development, although the patients' heights were still below the average for their ages. Sexual maturation developed satisfactorily, and puberty was manifested in all the patients who were of a puberal age. Psychological improvement was observed on a smaller scale; it was more noticeable in patients whose disease had started after the age of 1 year. In some of those who had congenital hypothyroidism a more or less marked oligophrenia persisted. The authors suggest that mental retardation resulted, in part, from lack of adequate education. They advise that such patients should receive special educational care, together with opotherapy.

Cold Injury in the Newborn: A Study of 70 Cases. B. D. Bower, L. F. Jones, and M. M. Weeks. Brit. M. J. 1:303-309 (Jan. 30) 1960 [London].

The authors classified 183 hypothermic newborn infants who were admitted to the Children's Hospital in Birmingham, England, between 1946 and 1956, according to the cause of their temperature reading below 96 F (35.6 C). Of these, 113 were classified as being premature, or having such conditions as cerebral birth injury, severe infection, congenital heart disease, perinatal asphyxia, severe malnutrition, and paroxysmal tachycardia, while 70 were classified as having primary cold injuries, the most important or only factor being external chilling. In 53 of the 70 children the minimum air temperature at the start of their illness was below 35 F (1.7 C); in 56 of the 70 infants the chilling occurred in the period between January and March. Other factors thought to be important are: delay in wrapping the infant after birth; tight wrapping, which may restrict muscular movement and peripheral circulation, and may act as an efficient insulator, keeping the infant cold when the room temperature rises; failure to heat the room at night; and inherent factors in the newborn infant. Nearly all the children were born at home, and since the average bedroom in England is heated inadequately or not at all, its temperature to a large extent reflects the external temperature.

The commonest symptoms in these children with cold injury were feeding difficulty, edema, coldness to touch, and lethargy. Symptoms dated from birth in 25 infants and from the first week of life in 60. The commonest signs on admission were edema in 54, immobility in 41, facial erythema in 31. and sclerema in 27. Oliguria was common in severe cases, and in a few patients a biochemical study was carried out which revealed elevated values of blood urea, phosphorus, and potassium. Treatment varied, but it soon became apparent that rapid warming could lead to hypothermia and convulsions, and the authors agree that warming should be slow. Eighteen infants died, a mortality of 25%. Pulmonary hemorrhage was a universal finding at autopsy. A follow-up survey of 36 of the 52 survivors showed that 92% were normal. One child had cerebral palsy, and 2 were mentally retarded to a mild degree. The prognosis, therefore, appears to be very good for infants who survive the initial attack of chilling. Probably all chilled babies should be admitted to hospital so as to have modern pediatric care, even though the details of treatment are still controversial.

Viremia in Infection Due to ECHO Virus Type 9. I. Yoshioka and D. M. Horstmann. New England J. Med. 262:224-228 (Feb. 4) 1960 [Boston].

The authors studied an institutional epidemic of infection with enteric cytopathogenic human orphan (ECHO) virus, type 9. Of 57 children, between the ages of 6 and 12 years, who resided in one of the cottages for retarded children, 42 had clinical symptoms of mild nonspecific febrile illnesses, 4 had symptoms of mild to moderately severe aseptic meningitis, and only 11 remained asymptomatic. With the aid of virus isolation from fecal and throat swabs and serologic tests, it became evident that virtually all the children were infected. Viremia was detected up to 6 days before the onset of fever in 10 of 18 children from whom blood samples were obtained in connection with other unrelated serologic studies several days before the epidemic began. Virus titers in the blood were low, the highest being 174 infection units per cubic centimeter of serum. In one of the patients with aseptic meningitis, ECHO 9 virus was isolated from the blood 3 days before the appearance of fever and 5 days before signs of involvement of the central nervous system developed.

Experimental infection was produced in 2 chimpanzees by feeding them a recently isolated strain of ECHO 9 virus. The only sign of infection in these animals was mild fever in one, coinciding with the peak titer of virus in the blood. The pattern of infection in man with viremia preceding clinical signs of the infection, the pattern of isolation of ECHO 9 virus from the throat and fecal specimens of infected persons, and the dynamics of infection in chimpanzees parallel the findings in poliomyelitis and suggest a similar pathogenesis of these 2 enteric infections.

Frequency of Accidents in Children. U-E. v. d. Leyen. Ztschr. Kinderh. 83:319-331 (no. 3) 1960 (In German) [Berlin].

The author reports on 771 boys and 506 girls with injuries sustained in accidents for which they were treated at the Children's Hospital in Hannover, Germany, in 1958. Of the 1,277 patients, 827 obtained a complete cure, 447 were improved, and 3 died of their injuries. Nine hundred and six patients were treated ambulatorily, and 411 were admitted to the hospital. The peak of the accidents occurred during the months of June to September. According to the type of accident, the patients were classified as follows: 13 who had suffered trauma at birth; 21 who were injured in their beds (including burns caused by hot water bottles and falls from the bed); 320 who had had accidents in the home (particularly falls on the stairs or the floor); 400 who had had accidents while playing; 328 who had had traffic accidents (most of them with injuries caused by collision with automobiles, motorcycles, and railroads); 159 who had had accidents in schools (many of them during exercises); and 36 who had swallowed foreign bodies.

Incised wounds were observed on 326 children, and 284 of them were operated on. All these patients were given tetanus antitoxin injections. Only 13 children had received tetanus vaccine. Tetanus occurred in a single patient, a 14-year-old boy with a wood-splinter injury of the leg, who had not been vaccinated and had not been given tetanus antitoxin. Of 247 children with head injuries, 96 had simple contusions of the head without involvement of brain or bones, 115 had brain concussions, 5 had brain contusions, and 31 had cranial fractures. Seven children had blunt injuries of the thorax, and 20 had blunt injuries of the abdomen; all of them recovered, and laparotomy was performed on only 1 patient. Bone fractures were sustained by 486 children; among these fractures the arm was involved in 243 cases, the clavicle in 60, and the tibia or fibula or both in 84. Healing occurred in most patients without complications and in good position. Dislocation of joints occurred in 55 patients, partial dislocation in 74, and contusions of extremities in 104.

The reported data show the high risk of accidents in childhood. Although the death ratio is small, almost every accident is associated with disturbances of the child's organism. Human beings in this stage of development show strong reactions, which are favorable with respect to healing but unfavorable mentally. The alteration of the psychic structure and the inhibition of development resulting from physical damage may be decisive for the future course of the child's life.

A Single-Dose Treatment of Threadworms in Children. R. H. R. White and J. W. Scopes. Lancet 1:256-257 (Jan. 30) 1960 [London].

Of 122 children with enterobiasis who were treated at the Evelina Children's Hospital in London, 59 were given Pripsen, a new granular compound containing piperazine phospate and standardized senna, and 63 children received piperazine phosphate only. Children between the ages of 2 and 5 years received 120 grains of Pripsen (which contains 45 grains [3 Gm.] of piperazine phosphate), while those between the ages of 6 and 12 years we given 160 grains of Pripsen (which contains grains [4 Gm.] of piperazine phosphate). Thoug both preparations were given as single doses 120 or 160 grains, the cure-rates (97% in thos children who received Pripsen and 92% in thos who received piperazine phosphate only) wer much the same as those reported with 7-da courses of piperazine. The doses of piperazine wer less than half those hitherto used in 7 days' treatment, and there were no toxic effects. Using single dose of piperazine-citrate elixir, other workers obtained a much lower cure-rate (43%). Further study is needed to elucidate the possible pharmacological advantages of the granular preparation of piperazine phosphate, as well as the precise part played by the senna component.

DERMATOLOGY

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Griseofulvin in the Treatment
Preliminary Report. A. G. Ochoa and
Gac. méd. México 89:1017-1024 (Nov.-Dec.) 1959 (In Spanish) [Mexico, D.F.].

Twenty patients, whose ages ranged from 4 to 8 years and who were suffering from different typ of dermatophytosis, were treated with griseofulvi The duration of the disease prior to treatmen varied from 2 weeks to 30 years. The diagnosis wa demonstrated in all cases by microscopic examina tion and, except in one case, by determination o the dermatophyte responsible for the infection Griseofulvin was administered in a dosage of 1 Gm daily, in tablets of 250 mg. each (one after each meal and one at bedtime). Children received half of the dose for adults. At the end of 2 months, 15 patients were cured of the infection on hairless skin, and 9 patients were cured of the infection on hairy skin. Those with tinea of the nails were progressing toward recovery at the time this article was written.

The first favorable changes under griseofulvin treatment, whether the lesions were those of tinea corporis, tinea cruris, or tinea pedis, were observed in the infection on hairless skin from the first week of therapy; they consisted in the disappearance of the pruritus, followed by decrease of the erythema and of scaling. Favorable changes were observed later in the lesions of tinea unguium; increase in the healthy area of the nail was observed in fingernails at the end of 4 weeks of treatment, and in toenails after a longer period. Side-effects were generalized pruritus in one patient, recurrence of colitis in another, and headache in 2. These reactions were not severe enough to cause interruption of the therapy.

INDUSTRIAL MEDICINE

Silicosis: II. Study of Sense of Taste and Pain Threshold. K. Yü-P'U and L. Yin-Tseng. Chinese M. J. 79:329-332 (Sept.-Oct.) 1959 (In English) [Peking].

The authors report on 417 patients, between the ages of 23 and 59 years, who were hospitalized in the Union Hospital in Peking, China; 278 of them [illegible] 56 were suspected of having silicosis. who were adn licosis associated with pulmonary Birmingham, I. these patients had been working cording to theth China, and had been exposed to below 96 F particles for periods ranging from 2 l as being prestimations of the sense of taste and cerebral birthreshold were made in these 417 pa- heart dise n 115 healthy men who served as con- ition and ation of the sense of taste was made by assified as l tongue with cotton swabs which had portant or in sugar solutions of various concentra- 53 of the 76ation of the pain threshold was made at the stal of a tubular device in which a needle, in 56 of th weight, could be brought perpendicu- period he contact with the skin to be tested. This test was applied to the flexor surface of the forearms, dorsum of the hands, and inner aspect of both thighs, and was repeated several times. The results showed that during the early stage of silicosis, even before there is definite radiologic evidence, there is an appreciable reduction in the ability to taste sweet substances and to feel pain, or an elevation of the respective thresholds has occurred. These observations confirm the known fact that patients with silicosis show disturbances of various types of analysors.

Silicosis: III. Study of Vegetative Functions. K. Yü-P'U and L. Yin-Tseng. Chinese M. J. 79:332-335 (Sept.-Oct.) 1959 (In English) [Peking].

The same group of patients with silicosis and the same healthy controls, reported on in the preceding paper, were studied by the authors regarding the reaction of the skin to ultraviolet irradiation. The dermographic reactions of the silicotics and of the controls also were studied. Both groups were subjected to water absorption tests, and their oculocardiac reflexes were studied. The results of these various examinations confirmed that patients with silicosis show a drop in autonomic nervous (vegatative) function (protective inhibition) in an early stage of their disease before a radiologic diagnosis of silicosis can be made. These findings, together with determination of the patient's occupation and his other symptoms, would be of value in the early diagnosis of silicosis.

Intoxication with Parathion in Agricultural Workers: Observations and Notes in 41 Cases. G. Battiato. Minerva med. 50:4086-4094 (Dec. 12) 1959 (In Italian) [Turin, Italy].

The author reports on 27 agricultural workers who were moderately or severely poisoned by the insecticide, Parathion. The most common symptoms of moderate intoxication, which appeared suddenly in these workers, were: abdominal pain; vomiting, frequently accompanied by vertigo; a slight degree of asthenia; headache; and bradycardia. Mild sweating was present in 7 patients, and mild fever in 11. The latter symptoms are apparently nonspecific, but to workers handling Parathion spraying substances, they are a warning of possible imminent eruption of the poisoning effects.

Severe intoxication with Parathion had similar initial symptoms as the instances of moderate intoxication, and the onset was sudden and acute. Unlike the moderate form, however, marked adynamia, impaired consciousness developing sometimes into coma, profuse sweating, pulmonary edema, and arterial hypertension appeared within 2 hours after the onset of the symptoms. The arterial hypertension gradually decreased, and became normal within a few days. It seems that the same quantity of Parathion may produce either moderate or severe symptoms of intoxication according to the individual reaction of the patient. Treatment with atropine is suggested at the onset of the symptoms, because initially it is not known whether a mild or a severe form of intoxication will follow.

THERAPEUTICS

Effects on Serum Lipoprotein Cholesterol of Estrogen in Combination with Delta-4-Androstenedione, Testosterone and Methyltestosterone. B. Hood and K. Cramér. Acta med. scandinav. 165:459-466 (no. 6) 1959 (In English) [Stockholm].

The authors cite earlier studies indicating that, when estrogenic and androgenic hormones were given simultaneously, estrogenic effects were eliminated or reversed. Their own studies were made on 9 patients. Five of these had survived one or more myocardial infarctions and had a total serum cholesterol value exceeding 300 mg. per 100 cc. before treatment. Two patients had hypercholesterolemia without definite evidence of myocardial infarction.

One of these had suffered a vascular cerebral insult at the age of 37 years and showed radiologic signs of aortic calcification at 38; he had no history of previous hypertension. Finally, the authors tested the action of androstenedione on 2 men with hypogonadism, one of whom showed the picture of Klinefelter's syndrome and the other had testicular atrophy after orchitis in connection with epidemic parotitis. The studies had the disadvantage that they were made on ambulatory patients. Moreover, the period of observation was probably not long enough, and the determinations were not made frequently enough.

Earlier studies on the shifts in values of lipoproteins in the Cohn fractions, caused by the administration of estrogen (ethinyl estradiol, dioxydiethylstilbene) as well as by the concurrent administration of estrogen and methyltestosterone, have been confirmed. Androstenedione (delta-4-androstene-3-17-dione) in a dosage twice that of methyltestosterone, however, did not have any effect in reversing the estrogen-induced pattern. Testosterone did not seem to differ from androstenedione in this respect, and androstenedione had no effect on the plasma cholesterol distribution pattern when given alone to 4 subjects (2 hypercholesterolemic men and 2 hypogonadic men).

Marked effects on the lipoprotein pattern in various studies have been found only with synthetic androgens, such as methyltestosterone, ethinyl. testosterone, and 17-methyl-19-nortestosterone. On the other hand, there was some evidence that naturally occurring androgens are not entirely without effect in this respect. The revirilizing effect of androstenedione in doses up to 100 mg. daily was not sufficient to be of decided practical advantage in men treated with as heavy an estrogen dose as 1 mg. of ethinyl estradiol daily.

Speed of Action of Aspirin, Soluble Aspirin and Buffered Aspirin. P. Sleight. Lancet 1:305-307 (Feb. 6) 1960 [London].

Six healthy volunteers, between the ages of 20 and 33 years, who had not taken any salicylate in the previous 72 hours, were given doses of 10 grains of 4 preparations of aspirin, namely, aspirin B.P., soluble aspirin B.P. (calcium aspirin), acetylsalicylic acid combined with aluminum carbonate and magnesium carbonate in small amounts (Bufferin), and acetylsalicylic acid combined with glycine (Paynocil), with use of a double-blind technique. Fifteen cubic centimeters of blood was drawn each time by repeated venipuncture at 0, 10, 20, and 30 minutes, the time recorded being the moment of venous occlusion. Blood levels of acetylsalicylic acid and salicylate were compared. Soluble aspirin B.P. gave about twice the blood levels of aspirin B.P. at these times, and equal levels were obtained with Paynocil and Bufferin, both of which were similarly superior to plain aspirin B.P. Suggested explanations are diminished local irritation and consequent speedier gastric emptying when soluble or buffered aspirins are used. The presence of unchanged acetylsalicylic acid has again been demonstrated in the serum; the significance of this observation is that aspirin therapy cannot be said to have failed, unless the drug has been taken at 2-or-3-hour intervals.

Diethylstilbestrol in Mumps Orchitis. E. Nordlander. Acta obst. et gynec. scandinav. 38:586-597 (no. 4) 1959 (In English) [Stockholm].

The author evaluated the results of diethylstilbestrol (Stilbestrol) therapy in 192 patients with mumps orchitis, admitted to the Stockholm Hospital for Infectious Diseases in Stockholm during 1948-1955. One hundred of the 192 patients received diethylstilbestrol by mouth in a dosage of 2 mg. 5 times a day for 3 days. The remaining 92 patients did not receive any treatment and served as a control group. There was no appreciable difference between the 2 groups in respect to the clinical course of the orchitis. Follow-up examinations of 61 treated and 56 untreated patients revealed pathologicoanatomic changes of varying degree of severity in 44 patients of the former and in 49 of the latter group,. but the difference was not statistically significant. Follow-up examinations of 38 treated patients, in whom semen analyses were carried out, and of 38 patients from the control group, in whom 67 analyses were performed, did not show any significant difference between the 2 groups in respect to the therapeutic effect of the drug on spermiogenesis. In this series diethylstilbestrol therapy had no noteworthy effect, either on the clinical course of orchitis or prophylactically in preventing the pathologicoanatomic sequelae in the affected testis. Nor did it prevent the disturbance of spermiogenetic function which usually follows orchitis and may cause a lowering of fertility.

The Relief of Pain in Osteitis Deformans (Paget's Disease of Bone) by Phenol Injection of the Sympathetic Chain. W. Reid. Scottish M. J. 5:71-75 (Feb.) 1960 [Glasgow].

Although pain is not a constant feature of Paget's osteitis deformans, it is not uncommon. When present, it may vary in intensity, and in some patients it is agonizing. The author became interested in this problem in 1948, when a woman demanded amputation for relief of pain associated with osteitis deformans of the right tibia. For a period of 4 years conservative treatment had failed to give relief, and the pain was now excruciating. Her request was refused at first as too radical, but some months later amputation was performed above the knee, and the patient was satisfied. Two years later she returned for treatment of a painful chronic ulcer of the left leg, which had developed after an injury. When conservative treatment did not relieve the ulcer pain, she suggested a second amputation.

Reasoning that the increased vascularity of the bone in Paget's disease might be responsible for the pain, the author decided to try the effect of a sympathetic block. Injection of procaine (Novocain) into the left side of the lumbar sympathetic chain resulted in complete relief of the pain. When the pain recurred, a watery 1:15 solution of phenol was injected around the lumbar sympathetic chain, and complete relief of pain resulted with healing of the ulcer. This has lasted for 8 years. Encouraged by this result, it was decided to treat other patients with painful osteitis with this method. It was found, however, that for relief to result, it was imperative to inject around the sympathetic chain at specific levels for pain in specific situations.

Data are tabulated on 16 patients with painful osteitis deformans, in whom the author resorted to the injection first of Novocain, and then of a watery 1:15 solution of phenol. The results of treatment have been satisfactory except in 4 patients in whom it was not possible to site the injection accurately because of extensive Paget's disease in the spine or deformity of the spine. The method is satisfactory when the disease affects the bones of the limbs, but it has not yet been used successfully when the spine and pelvis have been involved.

Hazards of Adrenocortical Therapy. W. T. Thompson and J. J. Kelly. Virginia M. Month. 87:80-83 (Feb.) 1960 [Richmond].

The authors selected at random from the 1957-1959 files of the McGuire Veterans Administration Hospital in Richmond, Va., the case histories of 70 patients on long-term adrenal steroid therapy and reviewed them for evidence of severe untoward reactions. Peptic ulcers occurred in 12 patients. Severe infections—3 fungal, 2 tuberculous, and 1 bacterial—were observed in 6 patients, 5 of whom died. Advanced osteoporosis was present in 5 patients, 1 of whom had paraplegia from compression fractures. Full-blown adrenal cortical hyperfunction (Cushing's syndrome) was observed in 4 patients. There were psychotic manifestations in 3 patients, severe edema in 3, and frank diabetes in 2. Arteritis developed in 3 patients treated for rheumatoid arthritis: the 1st patient presented with pancreatitis, pericarditis, pleuritis, and peripheral neuropathy; the 2nd had severe cerebral arteritis, peripheral neuropathy, and indolent skin ulcers; and the 3rd had a bleeding peptic ulcer, peripheral neuropathy, pericarditis, pleuritis, and chronic skin ulcers. All 3 patients improved slowly over a long period of time with gradual reduction and then cessation of steroid therapy. One patient with polyarteritis nodosa was relatively asymptomatic except for arthralgias; peripheral neuropathy and myocardial infarction occurred suddenly when steroid therapy was begun.

A total of 39 major ill-effects thus occurred in 35 of the 70 patients. It is evident then that, when used nonspecifically, adrenal steroids only suppress, never cure; that once a patient has been started on these drugs, especially for a chronic disease such as rheumatoid arthritis, it is very difficult, and often dangerous, to discontinue their administration; and that serious results may accompany use of the adrenal steroids. The decision to start a patient on nonspecific adrenal steroid therapy should be arrived at only after careful consideration of all the factors involved, weighing the possible benefits against the known ill-effects.

Effect on the Kidney of Drugs Containing Phenacetin. B. Harvald, F. Valdorf-Hansen, and A. Nielsen. Lancet 1:303-305 (Feb. 6) 1960 [London].

At the Bispebjerg Hospital in Copenhagen, the authors performed direct provocation experiments in a group of 27 patients who were acetophenetidin (phenacetin) addicts and whose renal function was reduced. Eleven patients were given acetophenetidin entirely free from acetic-4-chloranilide, 8 patients received an acetophenetidin preparation containing 0.13% of acetic-4-chloranilide, and 8 were given an acetophenetidin preparation containing 0.30% of acetic-4-chloranilide, a contaminant found in varying amounts in practically all preparations of acetophenetidin. For 3 days all drugs were withdrawn, and then the patients received 3 Gm. of the acetophenetidin preparations daily for 5 days. The nephrotoxic effect of acetophenetidin was estimated in the 27 patients by quantitative determination of the urinary sediment according to the Addis method. In the 11 patients given purified acetophenetidin, a slight, but not significant, rise was recorded in the erythrocyte and leukocyte counts in the urinary sediment; in the 16 patients given acetophenetidin contaminated with acetic-4-chloranilide, the effect was much more pronounced, with significant rise in both erythrocyte and leukocyte counts. As acetic-4-chloranilide is a much stronger former of methemoglobin than acetophenetidin, renal damage may be caused by the abnormal hemoglobins, and not by a direct toxic effect of acetophenetidin or related drugs.

PATHOLOGY

Antibiotic Combinations: Antibacterial Action of Serum After Ingestion of Novobiocin or Tetracycline or Both. H. A. Hirsch and M. Finland. New England J. Med. 262:209-214 (Feb. 4) 1960 [Boston].

The authors made a controlled study to determine the effect of the administration of novobiocin in combinations with tetracycline on the antibacterial activity of the serum of 8 healthy young men.

This activity was measured in a twofold-dilution test in broth with 4 test strains that were sensitive to one or both of these antibiotics. Synergistic effects of this combination in a 1:2 or 2:1 ratio were not observed in the contratests of the sensitivity of these strains in vitro, and the combined effect could be considered additive or indifferent. The same observations concerning the activity of the serum were made after ingestion of these antibiotics by the same persons in these ratios, as compared with the same amounts of the individual drugs. However, the administration of 500 mg. of tetracycline with 250 mg. of novobiocin resulted in a lower antibacterial activity in the serum against tetracycline-resistant staphylococci as compared with the dose of 250 mg. of novobiocin alone. These effects were confirmed by assays of the novobiocin and tetracycline content of the same serum done by an agar-diffusion technique employing different assay organisms.

Tumors of the Thoracic Bones. P. Bucalossi, S. Di Pietro and T. Rock. Tumori 45:695-750 (Nov.-Dec.) 1959 (In Italian) [Milan, Italy].

The authors survey the pathological and clinical problems characteristic of tumors of the thoracic bones and report on 34 patients (27 with tumor of a rib and 7 with tumor of the sternum) observed at the Cancer Institute of Milan. They point out that tumors of the thoracic bones are almost always of the malignant type, and that the chondromatous form prevails among tumors of the ribs, while plasmocytomas are more frequent among tumors of the sternum. Often the symptoms are not so severe even in malignant cases, and in many instances a precise diagnosis is possible only after histological examination. Surgery which consists of a wide removal of the affected rib, and often also of the adjoining ribs with the intervening tissue, is considered the therapy of choice. Suitable repairs of the residual gap are necessary in order to maintain the function of the thoracic wall. Radiotherapy is to be limited to patients with ablastic tumors and reticulosarcomas, to those in whom radical surgery is not possible, and to those with relapses after previous surgery.

An Evaluation of Hospital Infections with Analysis in Mortality and Morbidity. U. S. Veterans Administration Co-operative Study Committee for Hospital Infections. Surg. Gynec. & Obst. 110:157-163 (Feb.) 1960 [Chicago].

Hospital staffs are concerned with complications in patients due to infection with antibiotic-resistant organisms, particularly the staphylococci. The United States Veterans Administration division of research developed a cooperative study to evaluate this problem in 6 VA hospitals. Two hospitals are tuberculosis hospitals; a 3rd is a 150-bed general hospital in a small New England community; a 4th is a medium-sized (500-bed) general hospital in a university city of a quarter million; and the remaining 2 are university-affiliated general medical and surgical hospitals of 1,000 beds. To gather data, a basic form was developed for reporting each case of staphylococcic infection discovered in participating hospitals. From August, 1957, through January, 1959, i. e., during the 18 months of the cooperative study, 29,817 patients occupied 3,320 beds in the 6 VA hospitals. A total of 1,604 staphylococcic cultures were isolated from 1,261 persons, but 47 were taken from personnel in contact with the patients. There were 1,093 patients with clinical infections solely or dominantly due to staphylococci.

In this Veterans Administration study, quality of laboratory information has been assured by use of a reference center to establish standards and controls. A reference laboratory can distinguish early changes in types and patterns of infection as well as sensitivity of organisms to treatment. Bacteriophage typing is not necessary or desirable in all infections but should be accessible for study and control of local epidemics. Bed-by-bed rounds to identify infected cases are a useful spot check to provide baseline data for assaying the presence of epidemics or the effectiveness of control measures; this should be one function of a hospital infection committee. Approximately half of the infections in this study were found on the medical, and half on the surgical services. On each service about half of the patients entered with the infection, and half acquired it in the hospital. The frequency of staphylococcic infection in a hospital may be a fair index of the total reservoir of all bacterial infections in that hospital. No single instrument, substance, or maneuver can obviate infection or the need for application of an entire program of control measures, which must be developed with emphasis on phases specific to each institution.

Behavior of the Lipid Metabolism After Revascularization of the Ischemic Heart in the Dog. M. Ursini, A. Ciardiello, G. Curzio, and M. Grassi. Minerva chir. 14:1449-1457 (Dec. 15) 1959 (In Italian) [Turin, Italy].

The behavior of the total lipids, the phospholipids, and the cholesterol after myocardial revascularization was studied in 20 dogs. Tests were made on blood taken simultaneously from the venous coronary sinus, the right atrium, and the femoral artery before revascularization; this was repeated 1 to 24 months after revascularization. After the values of the total lipids, the phospholipids, and the cholesterol were determined in normal conditions, infarction was induced by ligation of the descending branch of the left anterior coronary artery, 10 to 15 cm. from the original point of the artery, and surgical revascularization was performed 8 to 10 weeks afterwards by ligation of the internal mammary arteries in the 3rd intercostal space, by pneumocardiopexis, by pericardiocardiopexis, or by a combination of the 3 methods.

Results showed that after the infarction there is some indication of a spontaneous recovery of the cardiac lipid metabolism. This recovery, however, is partial, and it is not observed in the phospholipids. Surgical revascularization caused a marked progressive improvement in the myocardial exchange of the lipids and especially of the phospholipid fraction. The best effects were observed in instances of isolated or associated bilateral ligation of the internal mammary arteries. Surgical revascularization caused a definite improvement in the lipid metabolism of the ischemic heart.

A Rapid (24 Hour) Bioassay for Detection of Human and Mouse Tumor Factor. *F. Friedman, R. Kassel, L. Burton, and others.* Proc. Soc. Exper. Biol. & Med. 103:16-19 (Jan.) 1960 [Utica, N. Y.].

A cell-free factor has been extracted and refined from human and mouse tumor tissue. This factor, when injected into C_3H (f) mice will induce a wide variety of tumors, i. e., parotid, mammary, and adrenal carcinomas, soft tissue tumors, and leukemia. For convenience, this factor has been designated as "tumor factor" (TF). The method utilized for extraction and refinement of mammalian TF is the Burton-Friedman-Kassel (BFK) procedure. This procedure is an adaptation of the method originally developed for purification of the tumor-inducing factor (TIF) present in the tu-e tumor strain of Drosophila melanogaster. Both methods were closely related, and past experience in the study of Drosophila tumors suggested that mammalian TF could produce in Drosophila the lesion already described in the literature as Drosophila tumor. Preliminary data concerning the reaction of Drosophila to refined mammalian TF indicated that Drosophila could be used as an assay animal for the rapid detection of mammalian TF. In this paper the authors describe the techniques and results of the Drosophila assay (DA) method. The Drosophila host line, wild 51-52, is a genetically stable and hardy strain. The preparations which were tested for the presence of TF by the DA method included, among others, serum, spleen, and lymph node material from patients with Hodgkin's disease; materials from mice with induced leukemia; pools of serum from groups of normal mice; and pools of serum from patients with various forms of malignancies.

The application of the DA techniques to materials obtained from mouse or human sources has indicated either the presence or the absence of TF. The presence of TF activity is computed from the number of surviving larval hosts which had developed melanotic lesions within 24 hours after injection. With one exception, all refined preparations which had TF activity in the DA induced neoplasia in mouse hosts. Absence of active TF in preparations, as indicated by the DA, was confirmed by lack of tumor induction by these preparations in C_3H (f) mice. The DA also did not detect any TF activity in the refined preparations from serums of 5 of 6 nonneoplastic human donors. Both Drosophila and mouse assays indicated absence of TF activity in procedural control preparations and Tris buffer. Crude BFK serum preparations of mouse and human TF induced formation of melanotic tumors in the injected wild 51-52 larvae. These DA results indicated that crude BFK preparations of pooled serum from 47 mice of the C_3H (f) (spontaneous tumor-resistant) line did not contain active TF, whereas active TF was present in crude BFK preparations of serum from patients with cancer and Hodgkin's disease. The use of larvae of the wild 51-52 strain of Drosophila as an animal assay has, among others, the advantages of (1) precise genetic control, (2) rapid indication of end-results (within 24 hours), and (3) ease of handling and maintenance.

RADIOLOGY

Mucormycosis. *O. F. Gabriele.* Am. J. Roentgenol. 83:227-235 (Feb) 1960 [Springfield, Ill.].

The author reports on 2 men and 1 woman, between the ages of 39 and 72 years, and on a 6½-year-old girl with mucormycosis, who had been admitted to the Grace-New Haven Community Hospital in New Haven, Conn., since 1955. In addition to mucormycosis, the 4 patients had diabetes mellitus, and in 2 it was poorly controlled. Large doses of antibiotics had been administered after the onset of clinical symptoms. All the patients died, and autopsies were performed on them. Mucormycosis is a rapidly fatal disease characterized by acute inflammation and vascular thrombosis, caused by invasion of the walls and lumens of blood vessels by the fungus. In cerebral mucormycosis, thrombosis of the internal carotid artery is common, and this finding was noted in 3 of the 4 patients. Other thromboses included the right ophthalmic vein in one of the men, the retinal artery in the girl, the ophthalmic artery in the other man, and the peripheral pulmonary artery in the woman.

In only one of the 4 patients was the pathogenic organism successfully cultured, and this revealed Rhizopus oryzae. In the woman the fungus could be visualized in the bronchial aspirate and tissues from the paranasal sinuses, but attempts to culture it were not successful. The diagnosis in the first 2 patients was established postmortem, and inability to obtain material suitable for culture made specific identification of the organism impossible. The clinical appearance of paranasal and cerebral involvement is characteristic, although this does not appear to be true of involvement of other organ systems. The cases of mucormycosis reported by other workers have almost invariably been associated with some underlying disease, usually diabetes mellitus (as in this series), but have included also leukemia (under treatment), nephritis, and cirrhosis.

The roentgenologic findings in the 4 patients were not diagnostic. Paranasal sinus disease was manifested by a clouded and thickened mucoperiosteum. Possibly the absence of fluid levels and the relatively unimpressive extent of the involvement of the paranasal sinus, as compared with the toxic state of the patient, may be characteristic. Pulmonary involvement was manifested as a lobular pneumonia with abscess formation and lack of response to therapy. Infarctions were not recognized as such. Although the roentgenographic changes are not characteristic, awareness of the entity and its association with predisposing metabolic disturbances may make it possible to consider the diagnosis while the disease is still in its controllable stage.

Epidemic Pulmonary Histoplasmosis: Roentgenographic Findings. D. P. Babbit and B. A. Waisbren. Am. J. Roentgenol. 83:236-250 (Feb.) 1960 [Springfield, Ill.].

The authors report roentgenographic findings on 18 male patients, between the ages of 15 and 71 years, and on a 58-year-old woman with epidemic pulmonary histoplasmosis, who were examined at the Milwaukee Hospital. The cause of the outbreak was established by the isolation of Histoplasma capsulatum from 2 of the 19 patients. In those patients in whom the illness and the chest lesions were very mild, lymphadenopathy with minimal pulmonary nodulation and infiltration was seen. In the others with moderate and severe lesions, the degree of hilar lymphadenopathy was more marked, and the nodulations and pulmonary infiltrations became more extensive with coalescence. Follow-up roentgenograms as long as 2½ years after the acute phase showed no evidence of calcification in these patients. About 3 to 5 years may elapse before calcification occurs.

Although the diagnosis cannot be made with certainty from the roentgenograms alone, it should be suspected. A history of possible exposure to H. capsulatum in the soil about 2 weeks preceding the occurrence of symptoms and roentgenographic findings should be highly suggestive. The diagnosis may be further corroborated by histoplasmin skin tests, complement-fixation tests, and biopsy of scalene lymph nodes to demonstrate the fungous agent. The findings are sufficiently suggestive to warrant their consideration in differential diagnosis among acute histoplasmosis, farmer's lung, sarcoidosis, noninfectious necrotizing granulomatosis, tuberculosis, metastatic malignant neoplasm, and other fungous diseases.

Idiopathic Pulmonary Hemosiderosis in Adults: Report of a Case and Review of the Literature. S. M. Bronson. Am. J. Roentgenol. 83:260-273 (Feb.) 1960 [Springfield, Ill.].

The author reports on a 27-year-old farmer with idiopathic pulmonary hemosiderosis, who was admitted to the Veterans Administration Hospital in Atlanta, Ga., because of weakness, pallor, dizziness, mild headache, and moderate dyspepsia. These symptoms, which were more marked on exertion, were of 6 months' duration. For 1½ months preceding the admission, the patient had had productive cough and hemoptysis associated with fever. The hemoglobin level was 9.8 Gm. per 100 cc.; the red blood cell count, 3.9 million per cubic millimeter; and the white blood cell count, 7,700 per cubic millimeter. Chest roentgenograms showed small nodular infiltrates in both perihilar lung fields, superimposed on a homogenous, finely granular background. These involved the mid and lower lung fields, and extended widely toward the lateral zones but not the subdiaphragmatic, costophrenic, and apical lung fields. A selective resorption of the infiltrates in the infraclavicular zones took place over a period of only 4 days, but densities in either lower lung field persisted. It was not until 2 months later that a chest roentgenogram showed marked clearing of either perihilar or infraclavicular densities with the appearance of a reticulostriate pattern in both mid and lower lung fields. No evidence of cardiac enlargement was observed. Bronchial washings showed the presence of macrophages containing hemosiderin, which had a Prussian blue reaction with potassium ferrocyanide.

During the major part of his hospital stay the patient was asymptomatic, but continued to have a mild degree of hemoptysis daily. After one month he was allowed to go home, but fever and increased hemoptysis occurred. On readmission, a lung biopsy was performed by open thoracotomy. A large number of intra-alveolar macrophages filled with iron were seen. A chest roentgenogram, obtained 6 weeks later, showed focal pleural thickening over the left pericardial lung field, with postsurgical adhesions of the left diaphragm. The pulmonary reticular markings persisted. Almost complete resorption of residual perihilar pulmonary densities was noted. A chest roentgenogram, obtained about a year later, showed no change in the appearance of the lung fields.

The cases of 34 adult patients with idiopathic pulmonary hemosiderosis were collected from the literature. A preponderance of men to women in the ratio of 2.7 to 1 was reported. The seriousness of the prognosis in this disease was revealed by the fact that 21 of the 34 patients were dead at the time of writing. The remaining 13 patients were alive for varying periods of 1 to 6 years when reported. All patients, on whom data were available, showed abnormal intrathoracic x-ray findings of pulmonary infiltrates, except for one patient who was followed clinically and roentgenographically for 11 months to death. It should be emphasized that the time interval over which the pulmonary infiltrates change is extremely variable. A negative chest roentgenogram on the 1st clinical observation of the symptomatic patient can be expected in about one-third of the cases, and does not rule out idiopathic pulmonary hemosiderosis. Pulmonary infiltrates, although present initially in two-thirds of the cases, may appear as late as 2½ to 5 years after onset of the clinical symptoms, but usually occur within 19 days to 2½ years. Hemoptysis, anemia with a hemoglobin level of 2 to 7 Gm. per 100 cc. (microcytic and hypochromic), persistent low serum iron value, and macrophages in the sputum containing hemosiderin are almost diagnostic of the disease. However, erythrocytosis may be seen intermittently in a patient who also shows, alternatively in his clinical course, a very low hemoglobin level or red blood cell count.

The radiologist has a unique opportunity and an important role in the diagnosis of idiopathic pulmonary hemosiderosis, if he is aware of the clinical aspects as he evaluates the chest roentgenogram. Although the list of differential diagnoses is impressive, careful scrutiny of the infiltrates, their distribution and variance in time, as well as the clinical laboratory data, will facilitate the correct diagnosis. In 29 of the 34 patients, the radiologist was able to suggest the diagnosis of idiopathic pulmonary hemosiderosis.

The Roentgenographic Appearance of Eosinophilic Lung (Tropical Eosinophilia). F. Y. Khoo and T. J. Danaraj. Am. J. Roentgenol. 83:251-259 (Feb.) 1960 [Springfield, Ill.].

The authors report on 550 patients with tropical eosinophilia, who were seen in the department of radiology of the General Hospital in Singapore. Although Singapore has a predominantly Chinese population, the disease was seen most frequently among Indians. Some of the patients were children and some were older persons, but the peak incidence was found in those between 20 and 40 years of age. The presenting symptom was chronic cough, which was most frequent and severe at night, occurring in paroxysms of a few minutes with mucoid or mucopurulent sputum sometimes streaked with blood. A detailed examination of chest roentgenograms revealed that the essential changes were increased lung markings of varying extent (appearing as fine, moderately thick, or rather coarse, massive strands) and mottlings associated sometimes with small areas of pneumonitis. It is felt that these changes are distinctive enough for a diagnosis to be made, especially in countries in which tropical eosinophilia is endemic. Of the 550 patients, an earlier group of 202 was treated with intravenous injections of oxophenarsine tartrate (Neo-Halarsine), and a more recent group of 348 was given oral treatment with diethylcarbamazine. Treatment with organic arsenicals or diethylcarbamazine resulted in a regression of the roentgenographic abnormalities.

Dilatation of the Aortic Sinuses in the Marfan Syndrome: Roentgen Findings in Five New Cases. I. Steinberg. Am. J. Roentgenol. 83:302-319 (Feb.) 1960 [Springfield, Ill.].

The author reports on 6 male patients, between the ages of 9 and 40 years, and on 4 female patients, between the ages of 2 and 47 years, with Marfan's syndrome; 5 of these patients had been reported previously, and 5 were new patients in whom a diagnosis of dilatation of the aortic sinuses (of Valsalva) was made with the aid of angiocardiography at the New York Hospital-Cornell Medical Center. Three of the 10 patients had aortic valvular insufficiency, and the other 7 had apical systolic murmurs. There were 3 deaths; 2 of the patients died of congestive heart failure associated with severe aortic insufficiency, and the 3rd died of uremia before significant enlargement of the heart and congestive heart failure had occurred. Seven patients were asymptomatic and were studied angiocardiographically and by cardiac catheterization.

Skeletal defects were present in all 10 patients; eye abnormalities were found in all but 2. In 6 patients family histories of Marfan's syndrome could not be elicited. However, when examinations of parents and siblings were made, the stigmas of Marfan's syndrome were evident. The blood pressure and electrocardiographic findings reflected the degree of cardiac involvement. Conventional chest roentgenograms readily disclosed deformities of the thoracic cage. Cardiac enlargement was evident in 8 patients. Roentgenograms also revealed abnormally long thoracic cavities, as well as long fingers and toes. Angiocardiography provided the definitive method of showing dilatation of the aortic sinuses, thus revealing the cardiovascular abnormality. In some patients angiocardiography provided the clue that linked the associated ocular and skeletal deformities. Nine of the 10 patients had uniform dilatations of the aortic sinuses, and in one who died and on whom autopsy was performed, the dilatation of the aortic sinus was aneurysmal and was associated with huge dilatation of the ascending aorta.

Marfan's syndrome is probably not as rare as had been previously supposed. The radiologist, by noting the unusually long and thin extremities, especially the fingers and toes, thoracic deformities, and cardiovascular abnormalities, may be the first to suggest the diagnosis, and thereby explain seemingly unrelated findings. The forme fruste type of Marfan's syndrome should be kept in mind whenever there is aneurysmal dilatation of the aortic sinuses or ascending aorta.

Cancer of the Thyroid from Roentgen-ray Therapy in Childhood. J. Perianes Carro, J. L. Pelaez Cueto, and G. Alonso Vivancos. Rev. clín. españ. 75:259-261 (Nov. 30) 1959 (In Spanish) [Madrid].

According to the literature, the incidence of cancer of the thyroid in adolescence is higher in those patients who have had roentgen-ray treatment of the upper thoracic or the cervical region in childhood than it is in those who have not had such treatment. Most frequently roentgenotherapy had been given to the patients for control of the symptoms of an enlarged thymus.

A 12-year-old girl was brought by her parents for consultation because of the development of apparently cardiovascular and respiratory symptoms which had become worse during the past 6 months. The patient had cyanosis (mainly in the lips and skin of the hands), dyspnea, rapid palpitation of the heart, and cough without expectoration. She was nervous, and her hands were perspiring and trembling. Her parents and 7 brothers and sisters were normal, although one sister had a goiter. The mother stated that the patient had had nodules over the thyroid region since the age of 2, and that between the ages of 2 and 5 she had had roentgen irradiation to the nodular area. She now had one large and several smaller nodules in the thyroid region. Roentgenologic examination of the chest showed nodules in the lungs, which were similar to those observed in patients with metastases of a seminoma or a Wilms tumor.

The test of seizure of iodine gave positive results in the skin of the thyroid region (250%) and strongly positive results in the skin of the metastatic areas of the right and left hemithoraces (360 and 290% respectively). The histological study of a surgically removed thyroid nodule showed carcinoma of moderate malignancy. The authors believe that in this patient a benign embryonal adenoma was stimulated by roentgenotherapy to develop into cancer.

PHYSIOLOGY

Oxygen Availability in Brain Tissues After Lipid Meals. R. L. Swank and H. Nakamura. Am. J. Physiol. 198:217-220 (Jan.) 1960 [Washington, D. C.].

Observations on erythrocytes in dark-field illumination demonstrated that large fat meals in dogs and in human subjects caused the red blood cells to become adhesive and to aggregate. Since these and other observations suggested that large fat meals may interfere with the diffusion of oxygen, the oxygen in the brain of hamsters was studied polarographically with the aid of permanently implanted platinum electrodes. It was found that, after the intake of large quantities of lipid, the amount of oxygen available in the tissues was reduced. The reduction was greatest after cream and other highly saturated fat mixtures. It was least after the very unsaturated oils, safflower and cod-liver oils. Changes after olive, corn, cottonseed, and other vegetable oils were intermediate. Cream meals, containing as little as 0.9 Gm. of lipid per kilogram of body weight, produced significant reductions in the available oxygen in the tissues.

The studies did not indicate that the unsaturated fatty acids, such as those contained in safflower and cod-liver oils, protect the organism from the effects of the saturated fatty acids. The oils caused less decrease in available oxygen in the tissues, but this appears to have been due to the fact that they contained less saturated fatty acids than the fats, and not to the presence in them of unsaturated fatty acids. In other studies, convulsive seizures were observed in hamsters after they had been fed cream in doses of 10 Gm. per kilogram of body weight. Oil feedings of the same amounts did not cause seizures. It seems likely that the reduction in oxygen availability after cream meals was an important cause of these seizures.

Blood Coagulation and Lipid Metabolism. F. C. Monkhouse. Am. J. Clin. Nutrition 8:1-6 (Jan.-Feb.) 1960 [New York].

Blood coagulation is the result of a complex series of reactions, and the formation of thromboplastin can be considered the 1st stage. The conversion of prothrombin to thrombin normally depends on the presence of thromboplastin, and thus can be considered the 2nd stage. Once thrombin is formed, it acts enzymatically to convert soluble fibrinogen to insoluble fibrin, and this reaction can be considered the 3rd stage. Associated with events in the 3rd stage of coagulation are the activation of plasminogen to plasmin and the subsequent lysis of fibrinogen and fibrin. This area has become highly specialized and complex and is not discussed in detail. One point, however, is relevant to the present discussion. It has been postulated that plasmin may function normally to prevent excess deposition of fibrin on the endothelium of the vessels.

Evidence is accumulating, which indicates that consumption of excessive amounts of fat or impairment in fat metabolism are factors in the development of atherosclerosis and thrombosis. The assumption that there is a relationship between blood clotting and thrombosis has led to an increasing number of studies on the role of fat in blood coagulation. After reviewing some of these studies, the author feels that it is reasonable to conclude that lipids, especially the phosphatides, play an important part in the formation of a blood clot. Not all lipids are coagulants. Changes in the level of fatty acids and phosphatides result in changes in a number of in vitro coagulation tests. However, variations in the same coagulation test can be demonstrated simply by varying the rate of centrifugation, the type of decalcifying agents, or even the order in which the reagents are added.

Thus, at present there is no clear understanding how changes in static blood are related to the development of an intravascular clot. It is unlikely that any changes in the coagulability of blood, brought about by variations in the lipid level, are important in the presence of a healthy endothelium or a normal blood flow rate. Such changes, however, may be significant when superimposed on degenerative changes in the vessel wall or when circulation is impaired. The clinical importance of lipids on blood clotting can only be ascertained when there is a better knowledge of the relationship between blood clotting and vascular changes.

Lipid-Induced Coagulation Changes in Normal Subjects and in Patients with Atherosclerosis. J. P. Dailey, E. A. Fullgrabe, R. L. Colescott, and Z. P. Tillotson. Am. J. Clin. Nutrition 8:34-37 (Jan.-Feb.) 1960 [New York].

After studies by other investigators had demonstrated an effect of a high-fat challenge on the integrity of red blood cells and on the rate of circulation in the peripheral vessels, the authors decided to investigate the effect of such a lipid challenge on the coagulation of whole blood at the times when these circulatory changes were taking place. Ten normal men were given 2 Gm. of fat (in the form of whipping cream) per kilogram of body weight after a fasting blood sample had been drawn. Additional blood samples were obtained at 2, 4, 6, 8, and 10 hours after the challenge. Chylomicrons, times of packing and distortion of red blood cells, and coagulation of whole blood were measured. Later the same subjects were challenged with 280 ml. of skimmed milk and 1,260 calories of carbohydrate. A lipid challenge with 2 Gm. of cream per kilogram of body weight was carried out also on patients (5 men and 5 women) who had had a cerebral vascular accident.

The authors found that the whole blood coagulation time after a lipid challenge was shortened in both normal subjects and patients with cerebrovascular disease. This effect was measured, utilizing a coagulation method of low inherent variability. The coagulation time curve had 2 depressions, one at 2 to 4 hours and the other at 6 to 8 hours after the challenge. The shortening in coagulation time at 2 to 4 hours after the ingestion of cream confirms earlier studies. The drop in coagulation time at 6 to 8 hours after the challenge corresponds to the time of maximum packing of red blood cells and decreased rate of circulation reported by Swank. This second shortening in coagulation time was greater in the older patient group than in the normal subjects. An isocaloric carbohydrate challenge to the normal group did not produce a similar alteration in coagulation time of whole blood.

Selective Extraction of Alpha-Cholesterol from Human Serum by Ethyl Ether. A. Katchalsky, B. Rosenzweig, J. Agmon, and M. Toor. Bull. Res. Counc. Israel. (Sec. E Exper. Med.) 8E:18-24 (Oct.) 1959 (In English) [Jerusalem].

During the investigation of cholesterol levels in various population groups of Israel, the authors corroborated observations previously reported by other workers that the variability in cholesterol levels could be attributed to the fraction bound with the electrophoretic beta-globulins, while the amount of cholesterol in the alpha fraction remained remarkably constant. In an attempt to distinguish between the alpha-cholesterol and the beta-cholesterol by an independent chemical method which would separate the 2 types of binding, it was shown that pure ethyl ether, when properly applied, can extract part of the total cholesterol in human blood serum selectively. A comparison with the results of electrophoretic fractionation showed that, in most of the cases, only the alpha-cholesterol and all of the alpha fraction had been extracted by the ethyl ether. Statistically significant correspondence between the ether extract and the alpha-cholesterol fraction was found in the blood of different population groups in Israel having widely different total cholesterol levels, as well as in the serums of patients with myocardial infarction and other diseases, such as nephrolithiasis, fever of unknown origin, bronchiectasis, leptospirosis, duodenal ulcer, thyrotoxicosis, and congenital heart disease, who showed a large variation in total cholesterol levels.

PUBLIC HEALTH

Q-Fever in New Jersey: Clinical and Epidemiologic Investigation of a Case with Some Unusual Manifestations. E. D. Pellegrino, R. F. Goldsboro, and O. Sussman. J. M. Soc. New Jersey 57:59-64 (Feb.) 1960 [Trenton].

This report is concerned with the first diagnosed case of Q fever in New Jersey, supported by laboratory isolation of the organism, Coxiella burnetii. The investigation revealed that the patient, a 35-year-old woman, had consumed raw milk from cows on a farm half a mile away. She also had had contact with the farm's newborn calves, the last time being 2 weeks prior to her illness. The patient exhibited unusual symptoms, not heretofore related to Q fever. Stomatitis, gingivitis, and cervical lymphadenopathy had been present for 10 days before she was admitted to the hospital, and she had not responded to treatment with penicillin. Throughout the illness she had experienced malaise, chilliness, and some anorexia. Her temperature rose to 102 F (38.8 C) shortly after admission, remained between 100 F (37.7 C) and 101 F (38.3 C) for 4 days, then dropped on the 5th day. Treatment consisted of the administration of 250 mg. of tetracycline 4 times a day and the use of alkaline mouth washes when needed. Symptoms gradually disappeared, with gradual subsidence of lymphadenopathy, increase in appetite, and a sense of well-being. There was no evidence of pulmonary infiltration, and the peripheral blood picture was essentially normal except for relative lymphocytosis. The patient's specific antibody titer for Q fever had been 1:256 during the course of the acute illness and subsided to 1.4 one year later.

The pathogenic agent, C. burnetii, was isolated from milk produced on the neighboring farm with which the patient had contact. Serologic evidence of infection was also obtained through blood testing. The exact mode of transmission of infection in the present study is not clear, since the patient's family had also consumed the raw milk and had not exhibited clinical symptoms or any elevation of complement-fixation titers for Q fever. It is not unlikely that the mode of transmission was related to the patient's contact with newborn calves, which she had fondled. This report is the first confirmed case of Q fever in a dairy herd in New Jersey and should alert clinicians to the possibility of this disease in the northeastern United States. Q fever should be considered in the differential diagnoses of fevers of obscure origin, even when contact with animals is quite indirect. Awareness of subclinical and atypical manifestations will result in greater recognition of Q fever, a disease which is increasing in public health and clinical importance.

Further Observations on the Course of the Diphtheritic Infection Based on the History of Hospitalized Patients in the Pediatric Clinic and on Reports of Patients Who Had Diphtheria in the Municipality of Florence from 1952 to 1958: Considerations and Plan of Prophylaxis with Combined Diphtheria and Tetanus Vaccinations. L. Nassi and C. Vecchi. Riv. clin. pediat. 64:285-305 (Oct.) 1959 (In Italian) [Florence, Italy].

The authors made a statistical study on the incidence of diphtheria among the children of Florence, Italy, during the period from 1952 to 1958 so as to determine the effectiveness of a vaccination program. There was a decreasing incidence of diphtheria throughout this period, from 430 instances in 1952 to 30 in 1956 and 25 in 1958. The mortality among patients treated for diphtheria in the pediatric clinic also declined; 6 patients died of this disease in 1952, 7 in 1953, 1 in 1954, and 1 in 1956, whereas none died in 1955, 1957, and 1958. These results are attributable to the effective diphtheria vaccination program which has been carried out in Florence. To maintain and to improve the achievement, the authors suggest the following time schedule of vaccinations for an infant—poliomyelitis vaccination: 1st administration at the 3rd month, 2nd at the 4th month, 3rd at the 9th month, and 4th at the 20th month; combined diphtheria and tetanus vaccination: 1st administration at the 6th month, 2nd at the 7th month, and 3rd at the 17th month.

Resistance of the Body Louse (Pediculus Humanus Corporis de G.) to DDT Powders. J. J. Steyn, J. J. de Beer, J. G. Greeff, and W. L. Coetzee. South African M. J. 34:90-92 (Jan. 30) 1960 [Cape Town].

Reports from numerous countries throughout the world indicate that in connection with typhus control the body louse can no longer be adequately controlled by DDT. Like the house fly, it has become resistant to this insecticide. The division of environmental sanitation of the World Health Organization (WHO) has arranged body-louse resistance tests with use of a standardized kit forwarded from Geneva. The investigations described were conducted at Queenstown, Union of South Africa, and in neighboring Bantu locations in Cape Province as part of a global survey. In 1954 and 1958 DDT powders from the standard WHO kit were used on cloth according to the kit instructions for determining the resistance of the body louse to these powders. In 1956 at Queenstown Dr. Carroll N. Smith, of the entomology research division, U. S. Department of Agriculture, confirmed the results obtained by the authors in 1954.

In September, 1954, resistance of the body louse to 5% DDT powder at Queenstown, where DDT had been regularly used at 6-week intervals since 1952, at Eskeaton, where less DDT had been used, and at Macibini, where still less DDT had been used, was found to be, respectively, 81.7, 56.7, and 5.0%. In August, 1958, at Qoqodala, where DDT had not been used for louse control, resistance to 1% DDT and 5% DDT was, respectively, 6.7 and 0%; at Matyantya, where DDT had not been used, resistance of the body louse to 1% DDT, 5% DDT, and 0.0016% pyrethrins was, respectively, 10, 0, and 6.7%. As the Queenstown lice were the most resistant of all the lice tested, but were still 100% killed by proper application of 10% DDT powder, it was suggested that experimental dusting of 2 or 3 premises, as well as of the occupants and their clothing, should be carried out to supplement future tests with the WHO test kit.

BOOK REVIEWS

Human Nutrition and Dietetics. By Sir Stanley Davidson, B.A., M.D., F.R.C.P.Ed., Professor of Medicine and Clinical Medicine, University of Edinburgh, A. P. Meikeljohn, M.A., B.Sc., D.M., Lecturer in Nutrition, University of Edinburgh, and R. Passmore, M.A., D.M., Reader in Physiology, University of Edinburgh. With foreword by Lord Boyd Orr, D.S.O., M.C., LL.D., F.R.S. Cloth. $15. Pp. 844, with illustrations. Williams & Wilkins Company, 428 E. Preston St., Baltimore 2; E. & S. Livingstone, Ltd., 16 and 17 Teviot Pl., Edinburgh 1, Scotland, 1959.

This book is a welcome addition to the subject of human nutrition. The authors are authorities whose backgrounds provide the broad prospective represented by the subjects included in the book. The volume is divided into six parts dealing with physiology, food, primary nutritional diseases, nutritional aspects and dietetic treatment of general diseases, public health, and diet and physiological stress. Despite the scope, the authors have succeeded admirably in selecting critical material for presentation, and they have condensed it into an orderly and readable discussion. In addition to the usual subjects which one might expect in a book of this title, they have considered a number of pertinent topics, including appetite and satiety, alcohol, the use of food tablets, beverages, herbs and spices, new and improved foods, food poisons (infective agents, chemical agents, natural poisons), diet and general disease, nutrition in malignant disease, athletics, effects of climate, diets for expeditions, and emergency rations.

The book is documented with well-chosen references which can serve as introductions for broader reading. These references are more international in character than one encounters in many books. The viewpoint and presentation will have wide appeal to public health workers, international nutritionists, educators concerned with disease patterns abroad, medical students, and physicians. Furthermore, this volume should serve as an excellent reference volume for nonphysician groups, such as dietitians, graduate students in physiology, biochemistry, and related subjects; food technologists; and agricultural workers concerned with nutrition.

The British dietary details will be less helpful to the American physician than to his British colleague. The discussions of pathology and of chemical findings in disease are too brief. In the chapter on cereals the author devotes too much space to wheat and less attention than is deserved to other important basic foodstuffs used in large quantity throughout the world. Similarly, the discussion on tubers inadequately treats cassava, yams, and taro. Those interested in tropical nutrition will note the absence of plantain in the discussion of important foods. These omissions are cited not to detract from this useful book but with the hope that they may be corrected in subsequent editions.

It is unfortunate that the authors have chosen to deal with the addition of chemicals in foods in a chapter entitled "Food Poisons: (2) Chemical Agents." One cannot label legitimate, desirable, chemical additives as food poisons. The ultraconservative attitude of the authors toward the use of nutrients produced in the laboratory to improve food products also detracts somewhat from the value of the volume.

The book is relatively free of errors and, despite the brief presentation of some subjects, it deserves widespread use as a textbook for courses in nutrition in schools of public health, medical schools, and university departments of nutrition and as a reference volume by many other groups.

William J. Darby, M.D.

Hemophilia and Other Hemorrhagic States: International Symposium, Rome. Editor: Kenneth M. Brinkhous, M.D. Professor of Pathology, University of North Carolina, Chapel Hill. Assistant Editor: Pietro de Nicola, M.D., Associate Professor, University of Pavia, Pavia, Italy. Cloth. $7.50. Pp. 266, with illustrations. University of North Carolina Press, Chapel Hill, 1959.

This symposium consists of 27 papers by 55 contributors presented before the Eighth Congress of the International Society of Hematology in 1958. The papers are in English and are well documented. They are based primarily on clinical and experimental work of the authors rather than on abstracts or summaries of the literature. There is a useful and necessary table of abbreviations. The articles are grouped under the subjects hemophilia (nature of the antihemophilia factor, treatment, and diagnosis), vascular hemophilia (pseudohemophilia A and B, Willebrand's disease, and Willebrand-Jürgens form), acquired hemophilioid states (Stuart clotting factor), the Hageman factor and surface reactions, factor X, and hemostasis in hemorrhagic crisis. The collection of papers brings together widely scattered material on the subject of coagulation, which is becoming more complex as each new observation is added. This book should be welcomed as a valuable contribution to the subject by all who are working in this field.

Raphael Isaacs, M.D.

QUESTIONS AND ANSWERS

USE OF BARIUM AND INTESTINAL OBSTRUCTION

To the Editor:—*It has been stated that barium should not be administered by mouth, unless through a Miller-Abbott tube, to a patient with intestinal obstruction. Does the same apply to methylglucamine diatrizoate?*

M.D., West Virginia.

Answer.—In the treatment of intestinal obstruction it is first necessary to determine whether the obstruction is in the colon or the small intestine. Giving barium by mouth is dangerous if the obstructing lesion is in the colon, since the barium suspension becomes inspissated in the colon and may increase the degree of obstruction. It may be necessary to give a barium enema first to be sure that the obstruction is not in the colon.

If the obstruction is not in the colon, and if the degree of obstruction is not sufficient to cause distended loops of small intestine (as seen in roentgenograms of the abdomen), it is safe to give barium by mouth, which method usually permits determination of the location and nature of the lesion. Barium suspensions do not become inspissated in the small intestine and therefore do not increase the degree of obstruction.

If the degree of obstruction is great enough to cause distention of the small intestine by gas and fluid, giving barium by mouth is not apt to be of assistance in determining the location or nature of the lesion. The barium suspension becomes diluted in the retained intestinal secretions and is not carried to the point of obstruction because of the altered peristaltic activity of the intestine. Since methylglucamine diatrizoate is an aqueous solution, its diluteness makes it an even less useful contrast medium than a barium suspension; therefore, it is rarely used. Sometimes attempts are made to gain information by administration of methylglucamine diatrizoate by intestinal intubation; this is usually fruitless, however, since the tip of the tube rarely reaches the site of obstruction and, again, dilution of the methylglucamine diatrizoate makes it a poor contrast medium.

TUBERCULOSIS ACQUIRED AT AUTOPSY

To the Editor:—*In the course of performing an autopsy a physician received a stab wound in the subcutaneous tissue of a middle finger. The lesion, which persists, has since been presumptively diagnosed as a tuberculous infection, since the subject of the autopsy had had fulminating pulmonary tuberculosis. The transitory healing of the wound was followed by the appearance of an isolated subcutaneous nodule at the wound site in 10 days, with gradually spreading subcutaneous edema and dusky cyanotic flushing of the skin. There has been no tenderness, erythema, or other sign of a pyogenic infection. There appeared to be a favorable response to treatment with streptomycin and isoniazid, but streptomycin therapy had to be discontinued because of vestibular reaction. Response (after eight days) to therapy with the sodium salt of para-aminosalicylic acid (PAS) and isoniazid is questionable, since the patient has developed intolerance to para-aminosalicylic acid. The efficacy of isoniazid therapy alone is questionable because of rapid mutation to resistant strains. Reliance on the response to natural processes, or the use of other chemotherapeutic agents, such as ethionamide (recently reported in the French literature), has been considered. I would appreciate comments and advice.* *M.D., New York.*

Answer.—An attempt should be made to confirm the diagnosis of tuberculosis by recovery of tubercle bacilli, although incision and drainage of the lesion may not be indicated. Should it break down or become fluctuant, however, the exudate should be cultured. If this is a tuberculous infection, a tuberculin test should give a positive result; however, the patient may have been tuberculin-positive prior to the accidental inoculation.

One is justified in treating such a lesion by antituberculosis chemotherapy in the absence of immediate confirmation. Isoniazid therapy in combination with streptomycin or para-aminosalicylic acid would provide a satisfactory regimen. The patient's reaction to streptomycin by irritation of the vestibular component of the eighth nerve is unfortunate, but, since return of vestibular function after use of streptomycin sulfate is usual, this toxicity may be discounted in the light of the seriousness of tuberculosis. If intolerance to para-aminosalicylic acid is severe, it may be necessary to discontinue its use, but a change to this drug's potassium or calcium salt may be tried.

The answers here published have been prepared by competent authorities. They do not, however, represent the opinions of any medical or other organization unless specifically so stated in the reply. Anonymous communications cannot be answered. Every letter must contain the writer's name and address, but these will be omitted on request.

If the use of both streptomycin and para-aminosalicylic acid becomes intolerable, the patient should be maintained on isoniazid in a daily dosage of 300 to 600 mg., with pyridoxine given concurrently, 50 mg. daily. This should be adequate therapy, unless the patient from whom the infection was acquired at autopsy had drug-resistant tubercle bacilli, either primarily or after chemotherapy. Recovery of tubercle bacilli and their study for in vitro susceptibility to the various antimicrobial agents would be of value. In the absence of significant tissue necrosis and a fluctuant lesion on the finger, the rapid emergence of isoniazid-resistant strains of bacilli is not likely. It is believed, however, that combination chemotherapy is superior to single-drug therapy. In addition to isoniazid, this patient might be given pyrazinamide, 2 Gm. daily. This drug has potential hepatotoxicity (after six to eight weeks of therapy), and liver function studies (determination of serum glutamic oxalacetic transaminase and sulfobromophthalein retention values) should be performed before initiation of therapy and every two weeks thereafter.

There would seem to be no reason for the use of iproniazid, which is similar to isoniazid but has a greater toxic potential. Other drugs, such as cycloserine, viomycin sulfate, thiocarbanidin, and ethionamide, are available but of limited usefulness, and some possess greater toxicity. The total duration of therapy, with use of isoniazid alone if problems with other drugs persist, should be a minimum of one year and probably 18 months.

CHRONIC URINARY TRACT INFECTION

To the Editor:—*Since the age of 2 years, a 6-year-old girl has had difficulties of the bladder consisting of intermittent episodes of pyuria, dysuria, frequency and urgency of urination, bed-wetting, and some stress incontinence. Pus cells have been found in her urine each time it has been examined during this four-year period. Numerous physicians have examined her, each giving cystitis as the only diagnosis. The results of roentgenographic studies of the bladder and kidneys and cystoscopic examination were normal, with the exception of typical inflammation of the mucosa of the bladder due to infection. Urine cultures have consistently produced Escherichia organisms of undetermined species. How should this patient be managed? Should she be given intensive therapy for a short time or continuous treatment over a long period?*

Henry C. Gorman, M.D., Smyrna, Ga.

Answer.—A careful reevaluation of this patient should be made. The most likely cause of continued cystitis in such a patient as described is a pathological lesion in the urethra such as a narrow meatus, urethral stricture, vesical neck contraction, or congenital anomaly. Recurrent pyuria in children also is likely to exist in the presence of vesicoureteral reflux which may be demonstrated by a properly made cystogram. Interstitial cystitis is also a distinct possibility. This entity can be suspected in the presence of diminished bladder capacity which is rather fixed in amount. Cystoscopy after overdistention of the bladder under anesthesia reveals typical submucosal hemorrhagic areas diagnostic of interstitial cystitis. If the cystitis symptoms are due to urethral pathology, correction of the pathological lesion should result in cure. If vesicoureteral reflux is present, an operation to eliminate such reflux is often necessary. Infravesical obstruction is almost sure to be present if vesicoureteral regurgitation is demonstrated. If reevaluation again fails to reveal the presence of a pathological lesion, control of the infection by administration of antibacterial medicine selected on the basis of culture and sensitivity tests is recommended. The administration of such drugs over a long period in urinary infections is not recommended, except in the presence of incorrigible anatomic defects causing obstruction or stasis.

MEDICAL ASPECTS OF RELIGIOUS DIETARY LAW

To the Editor:—*I would appreciate information or references regarding medical aspects of the Jewish dietary laws.* *M.D., Maine.*

Answer.—The Jewish dietary laws date from antiquity, but most authors seem to agree that these dietary restrictions were based primarily on a sound program of preventive medicine. The ancient Jewish priests have been referred to as the founders of prophylaxis. Although they are not known to have assumed the role of physicians they were adept in the diagnosis of and discrimination between such conditions as leprosy, diphtheria, and gonorrhea. The biblical references to leprosy, however, probably would include a varied group of skin diseases as we know them today.

These religious leaders are reputed to have performed autopsies on slaughtered animals to determine their fitness for consumption. Other dietary laws date from the Mosaic code developed during 40 years of wandering in the desert. These emphasized the danger of eating unfit foods, presented procedures for sanitary food preparation, and listed instructions for cooking, serving, and eating the various foods. There also were passages devoted to the benefits of moderation in living and to the dangers of overindulgence. These dietary laws indicate some knowledge of the physiology of digestion in their emphasis that animals which "cheweth the cud" were among those fit for consumption—the implication being that these animals digested their food more properly by virtue of regurgitation and rechewing, thus prolonging its exposure to salivary juice.

not definitely established but may be related to peripheral vasodilatation and increased blood viscosity. Generally it is relieved or improved after the red blood cell volume returns to normal, but this is not true of all patients.

Among the 266 patients with polycythemia vera there have been 29 cases of gout (10.9%). Eight of these patients (27.6%) complained of itching and were helped by control of both conditions. There has been less experience with primary gout, but generally the pruritis is controlled when the uric acid level is near normal levels. If probenecid is used, it should be remembered that this drug has been reported to cause pruritus without a skin rash.

Reference

Talbott, J. H.: Gout, ed. 2, New York, Grune & Stratton, Inc., 1957, pp. 1-39.

IMMUNIZING QUALITIES OF PRIMARY TUBERCULOSIS

To THE EDITOR:—*Does primary tuberculosis confer protection against, or produce increased susceptibility to, clinical tuberculosis?*

Jules Cooper, M.D., Woodbine, N. J.

ANSWER.—There is evidence that a person once inoculated with tuberculosis establishes a degree of resistance against new infection. This protection is incomplete, however. A small percentage of persons with primary infections develop progressive pulmonary tuberculosis or miliary and meningeal complications. Children who are known to be recent tuberculin converters or who are tuberculin-positive and less than 3 years old should be treated with either isoniazid alone or combined isoniazid and para-aminosalicylic acid, for a period of not less than one year, to lessen the possibility of such serious complications.

In spite of the "protection" offered by a positive tuberculin test result, clinical tuberculosis more often develops in persons with a positive tuberculin test result than in those who are suffering from their first infection. Tuberculosis control in the future will increasingly consist of long-term follow-up of all tuberculin-positive persons.

EFFECTS OF MIST IN INCUBATORS

To THE EDITOR:—*What is the efficacy of mist in an incubator in a nursery for newborn infants? The literature contains differences of opinion regarding its use for respiratory difficulties and hyaline membrane disease.*

John E. Brown, M.D., Corry, Pa.

ANSWER.—The use of mist to produce a supersaturated atmosphere in an incubator has not been conclusively shown to be effective in the prevention or treatment of respiratory difficulties and hyaline membrane disease. Atmospheres with relative humidities of 80 to 90% are reported to effect a lower death rate in premature infants compared with atmospheres with a relative humidity of from 30 to 60% (Silverman and Blanc, *Pediatrics* 20:477 [Sept.] 1957). Thus, if an incubator is so constructed that the addition of mist is necessary to achieve relative humidities of 80 to 90%, mist can be said to be beneficial to the infant.

FOOD VALUE OF TRIPE

To THE EDITOR:—*I have not been able to find information on the relative caloric value of fresh, pickled, or otherwise prepared tripe. A patient who is on a low-fat diet because of diabetes enjoys eating tripe and is unhappy since it is excluded from his diet. Should diabetics be allowed to eat tripe?*

M.D., Vermont.

ANSWER.—Bridges' "Food and Beverage Analyses" discloses that 115 Gm. (¼ lb.) of pickled tripe provides 70 calories and contains 1.4 Gm. of fat, 13.5 Gm. of protein, and 0.2 Gm. of carbohydrate. Canned beef tripe (115 Gm.) furnishes 170 calories and contains 9.8 Gm. of fat, 19.3 Gm. of protein, and no carbohydrate; 115 Gm. of stewed tripe contains 115 calories, 3.4 Gm. of fat, 20.7 Gm. of protein, and no carbohydrate. There are no figures for the vitamin and mineral content. Tripe could be used in a diabetic diet since it contains little or no carbohydrate.

SURGICAL CORRECTION OF INVERTED NIPPLES

To THE EDITOR:—*What types of plastic surgical procedures can be recommended for the correction of inverted or invaginated nipples?*

Benjamin F. Glasser, M.D., New Brunswick, N. J.

ANSWER.—There is no completely satisfactory operation for the correction of inverted nipples. All procedures involve use of local tissues, multiple incisions, and sutures around the periareolar area. In healing, the wounds tend to contract and pull the nipple back to its original status. One of the better procedures was described by Sellheim (*Zentralbl. f. Gynäk*, 41:305, 1917).

ACTIVATED CHARCOAL

To THE EDITOR:—*What is "activated" charcoal?*

Lester A. Crowell Jr., M.D., Lincolnton, N. C.

ANSWER.—Activated charcoal, also known as activated carbon or decolorizing carbon, is a fine, black, odorless powder which consists of at least 96% carbon. Activated charcoal is obtained by the destructive distillation of various organic materials, particularly wood and other plant materials. Sometimes it is chemically treated to increase its natural capacity for adsorbing organic coloring substances and nitrogenous base substances.

WASHINGTON NEWS

Designated Physicians for Pilots . .
Delay Asked on Health Bills . .
Self-Employed Retirement Measure Tax Relief Bill Signed . .
Experts Back Trade-Name Prescribing . .

FAA RULING ON PILOT PHYSICAL EXAMINATIONS

The Federal Aviation Agency decided that private, noncommercial pilots must be examined by specially designated physicians to qualify for their medical certificates.

Previously, any physician could perform the medical examination for such pilots. The new rule, which goes into effect June 15, means that all pilots, commercial and private, must go to physicians selected by the agency for their required physical check-ups.

The American Medical Association, the Aerospace Medical Association, the Flying Physicians Association, and the Civil Aviation Medical Association had backed the FAA's proposal that private pilots should be examined only by specially qualified and selected physicians.

The Aircraft Owners and Pilots Association was the chief opponent of the move. Among other things, the association said the requirement could work a hardship on persons who might have to travel great distances to obtain the physical examination from one of the 2,000 designated medical examiners (DME's).

However, the FAA contended that "there is no effective way of exercising administration over nondesignated medical examiners and there is no assurance that failures to apply the applicable standards will be discovered and corrected." A recent survey disclosed that 84% of private pilots awarded medical certificates did not meet the standards set by the agency, according to the FAA.

Noting that there will be a need for more DME's, the FAA said it "will welcome the application of any family physician who wishes to join us in our efforts to promote air safety." DME's are given courses of training on up-to-date knowledge of aviation medicine.

In issuing the new regulation, which had been the subject of months of hearings, the FAA said:

"It is clear that the public safety is directly threatened when the pilot of an aircraft is afflicted by a condition likely to produce sudden incapacity or which interferes with his abilities to perform with safety those duties necessary in the piloting of aircraft. The threat involves occupants on the ground as well as those of the aircraft, as demonstrated by several recent light plane accidents. The unindoctrinated physician cannot be expected to appreciate fully the air safety implications of many of the medical defects ordinarily compatible with the performance of other, nonflying types of activity.

"As a consequence, perfectly competent physicians have issued certificates to airmen with coronary heart disease, diabetes requiring insulin, potentially recurrent mental illness. These are conditions which medical specialists, who have carefully studied the involved safety implications, consider incompatible with safe flying. In the absence of a procedure which would permit adequate direction and supervision over the performance of examinations and issuance of medical certificates, it can be expected that airmen who do not meet the medical requirements will continue to receive certificates."

SEEK DELAY ON AGED HEALTH PLANS

The Health Insurance Association of America urged Congress to give a broad and deep study to proposals for financing medical care of the aged.

In a statement filed with the House Ways and Means Committee, the association said Congress should avoid hasty passage of a "costly and grossly inefficient" bill.

"There have been public hearings on only one of the numerous plans which have been introduced for congressional consideration," said the association, which represents health insurance companies of the nation. "This proposal was rejected overwhelmingly by the House Ways and Means Committee," said the group, referring to the Forand bill that would finance health care through the social security system.

"As regards all other plans before Congress, neither the facts nor public opinion have been adequately explored.

"Moreover, the whole issue has been exposed to intensified political pressures which are always brought to bear on legislation of this type in a presidential election year."

The association suggested that increases in existing benefits already being provided through state and federal public assistance programs might be the solution to the problem of health care of the aged rather than a costly new federal program. "There is no need for a new federal program," said the association.

A. M. A. ACCEPTS ADMINISTRATION PROPOSAL ON SELF-EMPLOYMENT RETIREMENT

The American Medical Association notified the Senate Finance Committee that it has no objection to the Administration's proposal that self-employed retirement legislation require that the self-employed participating in the program set up retirement savings plans for their employees.

(Continued on next page)

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References: 1. Ellison, R. R. and Burchenal, J. H.: J. Chronic Dis. 6:421 (Oct.) 1957. 2. Ultmann, J. E., Hyman, G. A., and Gellhorn, A.: J.A.M.A. 162:178 (Sept. 15) 1956. 3. Bethell, F. H.: J. Chronic Dis. 6:403 (Oct.) 1957.

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Tuckahoe, N. Y.

The Keogh-Simpson measure that passed the House last year and that is now before the Senate Finance Committee did not contain this provision. The over-all bill would permit self-employed persons such as lawyers, farmers, small businessmen, dentists, and physicians to defer taxes on 10% a year of income or $2,500, whichever is smaller, provided the money is placed in a qualified pension plan.

In a telegram to Sen. Harry F. Byrd (D., Va.), Chairman of the Committee, Dr. F. J. L. Blasingame, A. M. A. Executive Vice-president, said:

"This is to advise you that the American Medical Association has no objection to the Treasury alternative to H. R. 10 insofar as it suggests the inclusion of employees in retirement programs established by or for the self-employed."

The Finance Committee was expected to act favorably on the measure, and Senate passage appeared likely in view of widespread support. The bill is aimed at giving the self-employed similar tax treatment on retirement savings as now afforded salaried persons.

PRESIDENT SIGNS ELDERLY DEPENDENT BILL

President Eisenhower signed a bill allowing taxpayers a full deduction of medical and dental expenses paid for a dependent mother or father 65 years of age or older. Previously the deduction was limited to health costs of more than 3% of taxpayers' adjusted gross income.

The bill is expected to save taxpayers caring for their parents some 50 million dollars a year. The measure was strongly endorsed by the American Medical Association, which urged President Eisenhower to sign it despite some administration concern about the loss of revenue. In a telegram to the President, A. M. A. Executive Vice-president Dr. F. J. L. Blasingame noted that the Association "strongly supports" the bill. "We hope you will decide to sign this bill into law," the telegram stated. "This tax relief will help younger people who support elderly parents."

Late last year, the A. M. A. told Congress that to the extent the health problems of the elderly are economic in nature, further tax deductions should be considered.

EXPERTS TESTIFY ON PRESCRIPTIONS

Prominent drug experts told Congress that physicians should avoid prescribing drugs solely by generic name instead of by the brand name of the manufacturer. In testimony the Senate antitrust subcommittee studying drug industry pricing practices, most of the expert witnesses took issue with contentions that prescriptions should always list the generic term.

It would be "unsafe" to prescribe drugs by their broad generic name because of wide variations in quality of drugs on the present day market, said Dr. Lloyd C. Miller, a director of the U. S. Pharmacopia. He testified, that because of inadequate federal policing some drugs on the market bearing the industry's seal of approval fall below minimum medical standards. Until better quality control exists, it is unsafe for welfare patients and others to have their drugs prescribed at all times by generic name only, he said.

Dr. Newell Stewart, executive vice-president of the National Pharmaceutical Council, said substitution of different brands for a prescribed medicine could be "harmful" to the patient. "Drugs bearing the same generic name are not necessarily therapeutic equivalents," he said.

"Only the physician is qualified to diagnose his patient's illnesses and to prescribe the proper drugs," he testified. "Equally important, it is the physician, not the pharmacist, who knows the patient's history."

Dean Thomas W. Rowe of the University of Michigan College of Pharmacy said there should be no interference with present practices for prescribing medicines. Fewer than 1% of the drugs now on the market received federal inspection, he said. Of the percentage checked by the FDA, "over 5% depart in some significant manner from labeled specifications," said Rowe.

Rowe said most violations—"probably nearly all of them"—were made by small concerns with inadequate procedures for controlling production and with few or no trade-marked brands of their own.

Dr. Charles O. Wilson, Dean of the School of Pharmacy at Oregon State College, said it would be "extremely shortsighted" of physicians to prescribe only by generic name. He said there were significant differences in drugs because of the way they were made even though they were identical chemically.

Sen. Philip A. Hart (D., Mich.), a subcommittee member, said the testimony points to the need for continuous government inspection of drug manufacturing plants.

MISCELLANY

Dr. Henry Welch applied for retirement as Director of the Food and Drug Administration's Division of Antibiotics. Dr. Welch, who had been in ill health for some time, was the subject of the latest round of hearings before the Senate antitrust subcommittee. Committee investigators disclosed that Dr. Welch had earned $287,142 in income for the past 10 years from outside interests in private medical publications. The disclosure prompted Arthur S. Flemming, Secretary of Health, Education, and Welfare, to charge that Dr. Welch "deliberately misled his superiors" about the compensation he received from trade journals. He called for Dr. Welch's immediate resignation.

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A White House Committee of scientists proposed creation of a special advisory board to the Department of Health, Education, and Welfare to help prevent cancer-causing substances in food. "The rapidly increasing number of new chemicals potentially useful in agriculture and food production demand vigilant and careful scrutiny of the compounds offered in order to safeguard the consumer from those that may present carcinogenic and other hazards," said the committee that was appointed last year to study the use of chemical additives in food. The proposed advisory board of government and private scientists would help the HEW Department evaluate scientific data and decide whether to prohibit the use of possibly cancer-causing compounds.

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Facilities for complete and frequent blood counts must be available for patients receiving 'Leukeran', 'Myleran' or 'Purinethol'.

Full information about these products will be sent on request.

References: 1. Unugur, A., Schulman, E., and Dameshek, W.: New England J. Med. 256:727 (Apr. 18) 1957. 2. Burchenal, J. H., Karnofsky, D. A., Murphy, M. L., Ellison, R. R., Sykes, M. P., Tan, C. T. C., Mermann, A. C., Yuceoglu, M., and Rhoads, C. P.: Am. J. M. Sc. 228:371 (Oct.) 1954. 3. Altman, S. J., Haut, A., Cartwright, G. E., and Wintrobe, M. M.: Cancer 9:512 (May-June) 1956.

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MEETINGS

AMERICAN MEDICAL ASSOCIATION: Dr. F. J. L. Blasingame, 535 North Dearborn St., Chicago 10, Executive Vice-President.
1960 Annual Meeting, Miami Beach, Fla., June 13-17.
1960 Clinical Meeting, Washington, D. C., Nov. 28-Dec. 1.
1961 Annual Meeting, New York City, June 26-30.
1961 Clinical Meeting, Denver, Nov. 27-30.
1962 Annual Meeting, Chicago, June 11-15.
1962 Clinical Meeting, Los Angeles, Nov. 26-29.

AMERICAN

1960

May

American Gynecological Society, Williamsburg Inn, Williamsburg, Va., May 30-June 1. Dr. Andrew A. Marchetti, Georgetown Univ. Hosp., Washington 7, D. C., Secretary.

American Orthopaedic Association, The Homestead, Hot Springs, Va., May 30-June 2. Dr. Lee Ramsay Straub, 535 E. 70 St., New York 21, Secretary.

June

American Academy of Tuberculosis Physicians, Miami Beach, Fla., June 11. Dr. George P. Bailey, P. O. Box 7011, Denver 6, Secretary.

American Association of Neuropathologists, Statler-Hilton Hotel, Boston, June 11-12. Dr. Leon Roizin, 722 W. 168th St., New York 32, Secretary-Treasurer.

American College of Angiology, Roney Plaza Hotel, Miami Beach, Fla., June 10-12. Alfred Halpern, Ph.D., 11 Hampton Court, Great Neck, N. Y., Executive Secretary.

American College of Chest Physicians, Miami Beach, Fla., June 8-12. Mr. Murray Kornfeld, 112 E. Chestnut St., Chicago 11, Executive Director.

American Diabetes Association, Inc., Hotel Deauville, Miami Beach, Fla., June 11-12. Mr. J. Richard Connelly, 1 E. 45th St., New York 17, Executive Director.

American Electroencephalographic Society, Belmont Hotel, Cape Cod, Mass., June 10-12. Dr. George A. Ulett, 1420 Grattan St., St. Louis 4, Secretary.

American Geriatrics Society, Americana Hotel, Miami Beach, Fla., June 9-10. Dr. Richard J. Kraemer, 2907 Post Road, Warwick, R. I., Secretary.

American Medical Women's Association, Hotel Carillon, Miami Beach, Fla., June 9-12. Mrs. Lillian T. Majally, 1790 Broadway, New York 19, Executive Secretary.

American Neurological Association, Hotel Statler, Boston, June 13-15. Dr. Melvin D. Yahr, 710 W. 168th St., New York 32, Secretary.

American Physical Therapy Association, Penn-Sheraton Hotel, Pittsburgh, June 26-July 2. Miss Lucy Blair, 1790 Broadway, New York 19, Acting Executive Director.

American Physicians Art Association, Miami, June. Dr. Kurt F. Falkson, 7. E. 78th St., New York 21, Secretary.

American Rheumatism Association, Hotel Diplomat, Hollywood-by-the-Sea, Fla., June. Mr. Gerard W. Speyer, 10 Columbus Circle, New York City, Executive Secretary.

American Society of X-Ray Technicians, Netherland Hilton Hotel, Cincinnati, June 11-16. Genevieve J. Eilert, R.T., 16 Fourteenth St., Fond du Lac, Wis., Executive Secretary.

American Therapeutic Society, Barcelona Hotel, Miami Beach, Fla., June 9-12. Dr. Oscar B. Hunter Jr., 915 19th St., N. W., Washington 6, D. C., Secretary.

Association for Research in Ophthalmology, Inc., Miami, Fla., June 12-17. Dr. Lorand V. Johnson, 10515 Carnegie Ave., Cleveland 6, Secretary-Treasurer.

Endocrine Society, Eden Roc Hotel, Miami Beach, Fla., June 9-11. Dr. Henry H. Turner, 1200 N. Walker, Oklahoma City, Okla., Executive Secretary.

Idaho State Medical Association, Sun Valley, June 15-18. Mr. Armand L. Bird, Sonna Bldg., Boise, Idaho, Executive Secretary.

Maine Medical Association, Hotel Samoset, Rockland, June 19-21. Dr. Daniel F. Hanley, P. O. Box 240, Brunswick, Maine, Executive Director.

Northwest Proctologic Society, Roche Harbor, San Juan Island, Wash., June 21-24. Dr. L. D. Leslie, 1162 Willamette St., Eugene, Ore., Secretary-Treasurer.

Society of Biological Psychiatry, Deauville Hotel, Miami Beach, Fla., June 11-12. Dr. George N. Thompson, 2010 Wilshire Blvd., Los Angeles 57, Executive Secretary.

Society for Investigative Dermatology, Inc., di Lido Hotel, Miami Beach, Fla., June 13-15. Dr. Herman Beerman, 255 S. 17th St., Philadelphia 3, Secretary-Treasurer.

Society of Nuclear Medicine, Estes Park, Colo., June 22-25. Dr. Thad P. Sears, Veterans Administration Hospital, Denver 20, Chairman.

Society for Vascular Surgery, di Lido Hotel, Miami Beach, Fla., June 12. Dr. George H. Yeager, 314 Medical Arts Bldg., Baltimore 1, Secretary.

July

American Goiter Association, Church House, London, England, J 5-8. Dr. John C. McClintock, 702 Madison Ave., Albany 8, N. Secretary.

American Society of Facial Plastic Surgery, Hotel Elysee, New City, July 22. Dr. Samuel M. Bloom, 123 E. 83d St., New York Secretary.

Flying Physicians Association Hawaii Cruise, leaving Los Angeles San Francisco, July 11. For information write Mr. Mark E. D P. O. Box 3275, Tulsa, Okla.

Oregon Cancer Conference (Second Annual), Sheraton Hotel, P land, July 7-8. Dr. Martin A. Howard, 115 S. W. Taylor St., Portl 5, Ore., Chairman.

Rocky Mountain Cancer Conference, Hilton Hotel, Denver, July 20-21 Mr. Harvey T. Sethman, 835 Republic Bldg., Denver 2, Executive Se retary, Colorado State Medical Society.

August

American Association of Blood Banks, Jack Tar Hotel, San Francisc Aug. 21-26. For information write: AABB Central Office, Suite 161 30 N. Michigan, Chicago 2.

American Congress of Physical Medicine and Rehabilitation, Ma flower Hotel, Washington, D. C., Aug. 21-26. Mrs. Dorothea C. August 30 N. Michigan Ave, Chicago 2, Executive Secretary.

American Hospital Association, Civic Auditorium, San Francisco, Au 27-Sept. 1. Mr. Maurice J. Norby, 18 E. Division St., Chicago, Assist Director.

American Institute of Ultrasonics in Medicine, Statler-Hilton H Washington, D. C., Aug. 20. Dr. Dorothy M. Stillwell, Dept. of P Med. and Rehab., Univ. of Colorado Med. Center, Denver 20, Chairma

American Physiological Society, Stanford University, Calif., Aug. 2 26. Mr. Ray G. Daggs, 9650 Wisconsin Ave., Washington 14, D. C. Executive Secretary.

American Society of Clinical Hypnosis, Miami, Fla., Aug. 7-10. D Seymour Hershman, 6770 N. Lincoln Ave., Chicago 46, Secretary.

American Veterinary Medical Association, Denver-Hilton Hotel, Den ver, Aug. 15-18. H. E. Kingman Jr., 600 S. Michigan Avenue, Chic 5, Executive Secretary.

Biological Photographic Association, Inc., Utah Motor Lodge, S Lake City, Utah, Aug. 23-26. Miss Jane H. Waters, Box 1668, Gr. Central P. O., New York 17, Executive Secretary.

Conference on the Chemical Organization of Cells: Normal a Abnormal, University of Wisconsin, Madison, Aug. 25-27. Dr. J. F. McManus, Dept. of Pathology, University of Alabama Medical Ce Birmingham, Chairman.

Gerontological Society, Inc., Mark Hopkins Hotel, San Francisco, A 7-12. Mrs. Marjorie Adler, 660 S. Kingshighway Blvd., St. Louis Administrative Secretary.

National Medical Association, Inc., Penn-Sheraton Hotel, Pittsbu Aug. 8-11. Dr. John T. Givens, 1108 Church St., Norfolk, Va., Ex tive Secretary.

Reno Surgical Society, Mapes Hotel, Reno, Nev, Aug. 18-20. Dr. bert G. Lenz, 505 S. Arlington Ave., Reno, Nevada.

Rocky Mountain Radiological Society, Denver-Hilton Hotel, De Aug. 11-13. Dr. John H. Freed, 4200 E. 9th Ave., Denver 20, Secre Treasurer.

St. Joseph's Hospital Annual Clinics, St. Joseph's Hospital, De Aug. 3-5. Dr. W. H. Leitch, St. Joseph's Hospital, 1818 Humbold Denver 18, Chairman.

West Virginia State Medical Association, The Greenbrier, W Sulphur Springs, Aug. 25-27. Mr. Charles Lively, Box 1031, Char 24, W. Va., Executive Secretary.

September

American Academy of Pediatrics, and American Academy of eral Practice, Louisiana Chapter, Roosevelt Hotel, New Or Sept. 23. Dr. Herbert B, Rothschild, 1520 Louisiana Ave., New O 15, Chairman of Publicity Committee.

American Medical Writers' Association, Hotel Morrison, Ch Sept. 30-Oct. 1. Dr. Harold Swanberg, 510 Maine St., Quincy, Secretary.

American Roentgen Ray Society, Ambassador Hotel, Atlantic Sept. 27-30. Mr. Hugh Jones, 20 N. Wacker Dr., Chicago 6, Di Public Relations.

American Society of Clinical Pathologists, Palmer House, Ch Sept. 24-Oct. 2. Mr. Claude E. Wells, 445 Lake Shore Drive, Ch 11, Executive Secretary.

College of American Pathologists, Palmer House, Chicago, Sept 27. Dr. Arthur H. Dearing, 2115 Prudential Plaza, Chicago, Exe Director.

Colorado State Medical Society, Stanley Hotel, Estes Park, Sept 17. Mr. Harvey T. Sethman, 835 Republic Bldg., Denver 2, Exe Secretary.

Delaware, Medical Society of, Rehoboth, Del., Sept. Mr. Law C. Morris Jr., 1925 Lovering Ave., Wilmington 6, Del., Exe Secretary.

Flying Physicians Association, third clinical meeting, Western Lodge, Wagoner, Okla., Sept. 6-9. For information write: Flying cians Association National Headquarters, P. O. Box 3275, Tulsa,

Inter-Society Cytology Council, Palmer House, Chicago, Sept. Dr. Paul A. Younge, 1101 Beacon St., Brookline 46, Mass., Secr

(Continued on page 34)

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PULMONARY ALVEOLAR PROTEINOSIS

REPORT OF CASE WITH FATAL OUTCOME

Edgar G. Harrison Jr., M.D., Matthew B. Divertie, M.D.
and
Arthur M. Olsen, M.D., Rochester, Minn.

Pulmonary alveolar proteinosis, apparently a new disease, is being encountered with increasing frequency. Clinically, progressive dyspnea is a common feature, and its severity is often at variance with the extent of the roentgenographic changes, which frequently resemble those of pulmonary edema. Pathologically, the alveoli are filled with a dense material that gives positive results when subjected to the periodic acid-Schiff staining technique; this material contains abundant fat and apparently is produced by proliferation and degeneration of septal cells. The pathogenesis of this disease and the exact nature of this material are obscure. This case represents the ninth fatality among the 32 cases of this disease now available for review in the literature.

SINCE pulmonary alveolar proteinosis was first described in June, 1958, we have been able to find reference to only 32 cases in the world literature; 27 of these were included in the original report of Rosen and associates.[1] The characteristic pathological changes in the lung were recognized as early as 1953, before the entity was delineated, and the condition will no doubt be diagnosed with increasing frequency in the future. The final diagnosis depends on the microscopic demonstration in the alveoli and smaller bronchioles of a dense, granular or floccular acidophilic material that gives a positive reaction in preparations stained by the periodic acid–Schiff (PAS) method. Although this amorphous material has been described as proteinaceous, its true chemical composition is unknown. The disease is one of unknown cause, variable course, and uncertain outcome.

This report concerns a case of pulmonary alveolar proteinosis in which death occurred within five months of the onset of progressive pulmonary insufficiency. It brings the total number of recorded deaths from this disease to nine.

Report of Case

History.—A 42-year-old man, a wholesale fruit merchant from the state of Washington, was first seen at the Mayo Clinic on March 6, 1959. He gave a four-month history of nonproductive cough and increasing dyspnea and cyanosis on exertion. Although he came from a region of pine forests, he had not worked with lumber nor was he exposed to any known pulmonary irritant. He had been in good health until seven months previously, when he noted the onset of a chronic cough associated with fatigue and some fever. This lasted for six

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weeks and finally cleared up after one injection of penicillin. He remained well during the next three months and then experienced the gradual onset of dyspnea on exertion. Subsequently, he had a nonproductive cough, tightness in the thorax, and fatigue and cyanosis which worsened with effort.

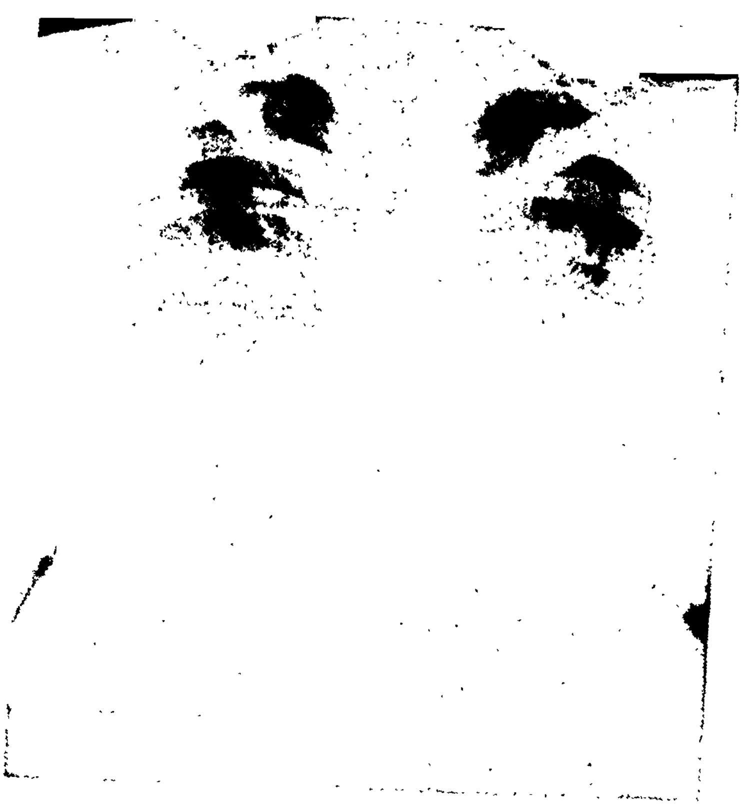

Fig. 1.—Pulmonary alveolar proteinosis: roentgenographic appearance, showing involvement of both lung fields by diffuse, finely nodular, soft densities of predominantly perihilar and basal distribution. Absence of hilar or paratracheal adenopathy and of significant cardiac enlargement is noteworthy.

His symptoms progressed and were not relieved by cessation of smoking and by taking 100 mg. of cortisone daily. He was found to have an abnormal thoracic roentgenogram and, in February, 1959, biopsy of a right-sided scalene lymph node was performed elsewhere. Histologically, the node showed only inflammatory change. The dose of cortisone was increased to 300 mg. per day, but his tolerance for exercise gradually became reduced by dyspnea to half of one city block at a normal pace. In the two weeks prior to his examination here, he had frontal headache and retro-orbital aching, which were relieved by therapy with acetylsalicylic acid.

Results of Examination.—Examination at the clinic revealed severe dyspnea during normal conversation. The pulse rate was 120 beats per minute, with a regular rhythm. The blood pressure and temperature were normal. He was extremely cyanotic, and there were telangiectases and livid and cyanotic papules over the upper part of the trunk. Early clubbing of the fingers was noted. Fine crepitations were present throughout both lung fields. Funduscopic examination revealed greatly distended veins with normal pulsations. The optic disks appeared hyperemic and full.

The value for hemoglobin was 18.8 Gm. per 100 ml. of blood, and the hematocrit value (volume of packed cells) was 69%. Leukocytes numbered 12,600 per cubic millimeter, with a normal differential count. A blood smear showed piling of erythrocytes and mild polychromasia. Serum electrophoresis disclosed an increase in alpha$_2$ globulin. Values for the erythrocytic sedimentation rate and plasma carbon dioxide were normal. Skin tests with first-strength and second-strength tuberculin and with histoplasmin, serologic tests for syphilis, the L. E. clot test, and examination of the sputum for malignant cells and acid-fast bacilli all gave negative results. A 12-lead electrocardiogram was interpreted as being within normal limits. The veno pressure was 20 cm. of water.

A roentgenogram of the thorax revealed bilater diffuse changes suggestive of pulmonary edema b compatible with a diffuse inflammatory or fibrot process (fig. 1). Moderate elevation of the righ hemidiaphragm was present. Results of pulmonary function tests showed deviations from predicte normal values compatible with diminished pulmonary volumes and severe difficulty in diffusio (see the table). Desaturation of arterial oxygen occurred during exercise while the patient was breathing 100% oxygen, and it was thought likely that this was on the basis of a right-to-left shunt at the atrial level through a valve-competent, probe-patent foramen ovale. This was thought to result from increased pressure in the right side of the heart, secondary to obstructive disease of the lungs. It was obvious that he had severe respiratory insufficiency, with secondary polycythemia and probably cor pulmonale.

Pulmonary Function Data in Patient with Pulmonary Alveolar Proteinosis

Entity Measured	Estimated Normal	Value in Patient
Pulmonary volumes		
Vital capacity	4.7 liter	2.19 (2.30)* liter
Residual volume	1.6 liter	1.01 liter
Total capacity	6.3 liter	3.20 liter
Residual volume/total capacity × 100	<35%	32%
Functional residual capacity	2.8 liter	1.49 liter
Inspiratory capacity	3.5 liter	1.79 liter
Expiratory reserve	1.2 liter	0.18 liter
Maximal breathing capacity	127 liter/minute	155 (165*) liter/minut
Expiratory slowing	0	0(0*)
Air trapping	0	0(0*)
Nitrogen washout index	2.5% or less	0.4%
Arterial oxygen saturation (oximeter)		
Resting	95-98%	79%
Breathing oxygen	100%	100%
Before exercise	95-98%	75%
Exercise for 0.9 min.	No fall	65%
0.5 min. after exercise	...	60%
Exercise (oxygen) for 1.6 min.	100%	91%
Ventilation breathing oxygen (at rest)		
Liters per minute	...	12.49
Rate: respirations per minute	...	15.6
Average tidal volume (ml.)	...	800

* Values after use of aerosolized bronchodilator.

Diagnosis.—The diagnosis was thought to be either the Hamman-Rich syndrome, alveolar cell carcinoma, or alveolar proteinosis, with the first of these considered as most likely. The changes in the skin and optic fundus were considered to be caused by the polycythemia. The severe respiratory insufficiency contraindicated biopsy of the lung.

Therapy.—Because of rapid deterioration in the patient's condition while undergoing examination, he was hospitalized and treated with a low-sodium diet, digitalis, diuretics, intermittent oxygen therapy, and phlebotomies. Dexamethasone in daily doses of 4.5 mg. and antibiotics for low-grade fever also were used. On this regimen, he lost 18 lb. (8.2 kg) in body weight and his hemoglobin level was reduced to 12.6 Gm. per 100 cc. No demonstrable changes in the appearance of the thoracic roentgenograms were noted after this treatment. The patient was allowed to go home after two weeks in the hospital. He was feeling more comfortable but was given an extremely guarded prognosis. He died one month later.

Pathological Findings

Post Mortem.—Autopsy was performed elsewhere. The major findings were those of cor pulmonale and a diffuse process involving both lungs. The combined weight of the lungs was 2,692 Gm. (5.6 lb.). They presented diffusely mottled, yellowish-tan surfaces and contained palpable firm miliary nodules, each a few millimeters in diameter, within the parenchyma.

The pathological changes in this patient's lungs were similar to those described previously in cases of pulmonary alveolar proteinosis. The cut surface of the pulmonary parenchyma showed coalescent grayish zones of consolidation, with irregular brown mottling; the intervening parenchyma appeared somewhat emphysematous (fig. 2).

Microscopic examination showed that the consolidated appearance of the gross specimen was caused by a dense, relatively acellular, eosinophilic material that filled the alveoli (fig. 3*a*). There was no inflammatory reaction or fibrous thickening of the interalveolar septums in most of the sections examined. The floccular and granular material gave an intensely positive reaction with the periodic acid–Schiff technique, and some PAS-positive material was also present in the septal cells (fig. 3*b*). Acicular needle-like spaces were present within the material. In frozen sections viewed by polarized light, these clefts were doubly refractile because of their content of lipids. This proteinaceous material apparently was formed by the proliferation, desquamation, and degeneration of alveolar septal cells (fig. 3*c*). Some of the degenerated cells produced rounded masses, a number of which had a laminated structure.

Staining with Sudan IV demonstrated fat within the foamy cells that in some locations filled the alveoli and within the intra-alveolar material. Mucicarmine stains did not demonstrate mucus within this material. These foamy cells also contained cytoplasmic granules demonstrated by the PAS-method, and they degenerated and contributed to the intra-alveolar material (fig. 3*d*). As a terminal event in this case, pulmonary emboli were present in sections of small arteries. Foci of superimposed recent pneumonitis also were noted (fig. 4). Lysis of the proteinaceous material by the inflammatory reaction was present in these regions of pneumonitis. Fungi or other parasites were not found in this tissue when it was stained by Gomori's methenamine–silver nitrate technique (Grocott's modification).

Sputum Studies.—Since some patients with alveolar proteinosis may have pulmonary insufficiency of such severity as to make biopsy of the lung impossible, as in the present instance, some diagnostic aid might be obtained by histological and histochemical studies of sputum. We decolorized smears of this patient's sputum that previously had been stained by the Papanicolaou procedure. The amorphous material on the slides still turned a deep red with the PAS method and stained only slightly with mucicarmine. The characteristic cellular reaction was not found. Five control sputums of patients screened for presence of malignant cells were processed in the same way. These mucoid sputums also turned red with the PAS technique, and they contained more material staining with mucicarmine than did the sputum of the patient who had proteinosis. However, this difference was considered inconclusive evidence of this disease, even in retrospect. Perhaps after more cases are encountered, it may be found that histochemical procedures and study of sections of unsmeared thick sputum may be of assistance in making the diagnosis when pulmonary biopsy is not feasible. At present, examination of tissue is the only certain way to establish the diagnosis.

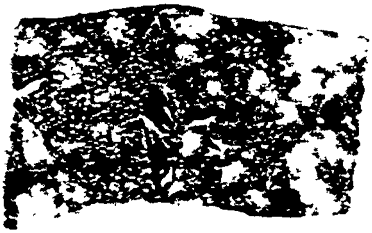

Fig. 2.—Cut surface of formalin-fixed lung tissue, showing coalescent zones of consolidation, with emphysematous appearance in intervening tissue.

Comment

Pulmonary alveolar proteinosis is predominantly a disease of adult males. Despite the constancy of the pathological changes in the lungs, the clinical picture is variable. Often, little correlation is seen between the appearance of successive roentgenograms and the progress of the patient. Improvement or worsening of the clinical picture often may be accompanied by paradoxical changes in the thoracic roentgenogram. By far the earliest and most prominent symptom has been dyspnea on exertion. Cough, with or without sputum, fatigue, thoracic tightness or pain apparently related to the effort of breathing, and mild loss of weight have been frequent complaints. Cyanosis was an early feature in all the patients who died. In most instances, the course has been afebrile; however, as

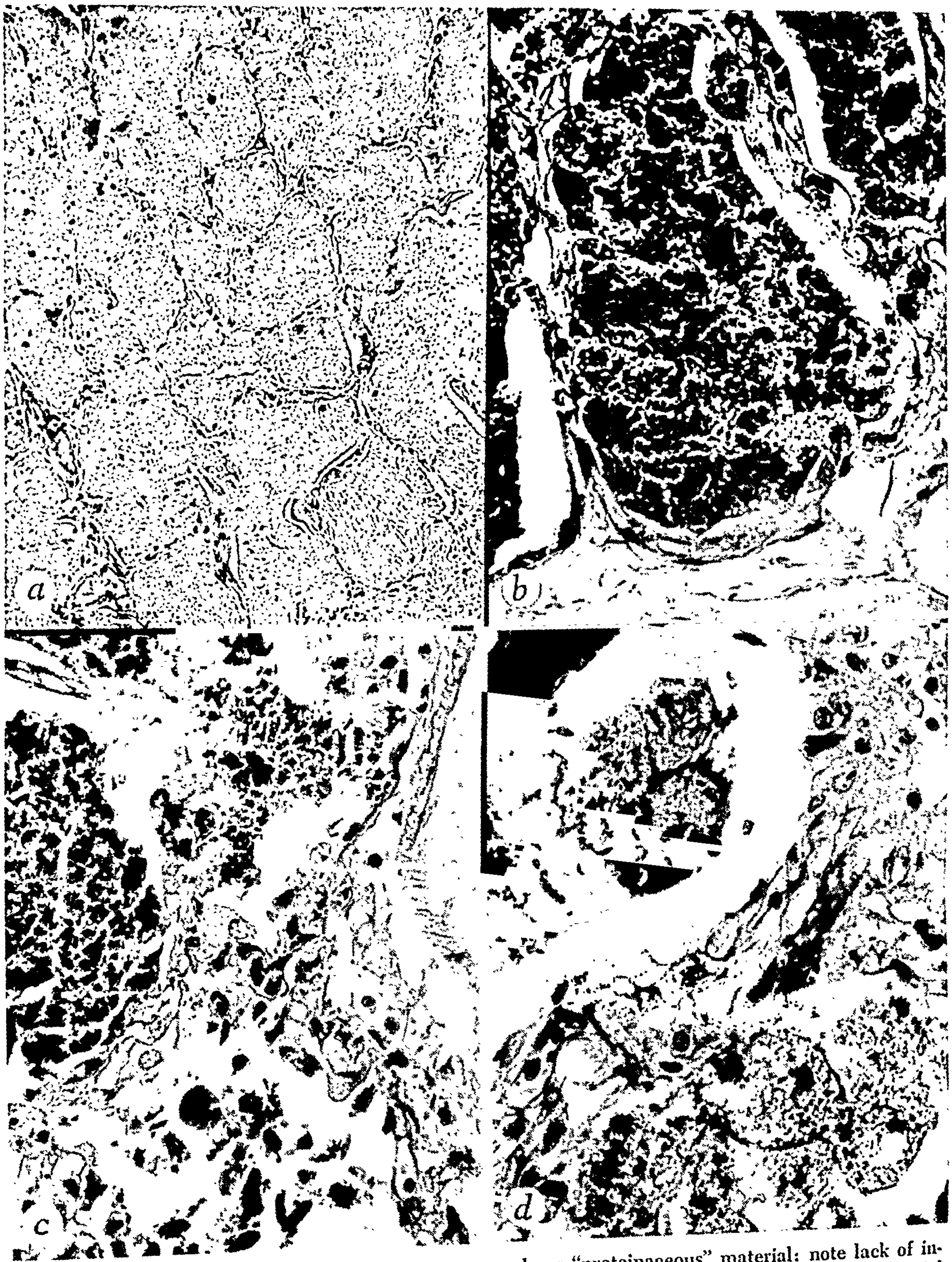

Fig. 3. *a*, pulmonary alveoli filled with dense amorphous "proteinaceous" material: note lack of interstitial fibrosis or inflammatory reaction (hematoxylin and eosin stain; × 100). *b*, amorphous material filling alveoli appears more granular and floccular with (PAS) periodic acid–Schiff technique. Some PAS-positive material also is seen in cells lining alveoli; note acicular spaces within material (PAS stain; × 400). *c*, proliferation, desquamation, and degeneration of septal cells on an interalveolar septum: note rounded body in lower middle part formed from a degenerated cell (PAS stain; × 380). *d*, cells containing fat and PAS-positive granules have degenerated and contributed to amorphous intra-alveolar material (PAS stain; × 450).

in the present case, a premonitory febrile respiratory illness has been noted on occasions. Moertel and co-workers[2] reported a case with features of a systemic disease in which the main problem was fever of unknown origin that responded well to steroid therapy. In several cases in which death occurred, secondary bacterial or fungal infection has been seen, probably facilitated by steroid and antibiotic therapy.

At most, a few scattered rales may be heard on examination of the thorax. The physical signs in the lungs are extremely meager in comparison with the extensive disease seen in thoracic roentgenograms. The roentgenographic changes tend to be mainly perihilar or basal in distribution; although they closely resemble the changes of pulmonary edema, none of the clinical stigmata of that disorder are present. Similar changes may be present in sarcoidosis, but the hilar adenopathy so characteristic of this disease has not been described in alveolar proteinosis. Calcification of the lesions has not been observed.

Laboratory studies have not been helpful, but polycythemia and nonspecific changes in the globulin fractions of the serum have occurred in a few instances. Pulmonary-function tests have given results ranging from normal measurements in the presence of extensive changes in the thoracic roentgenogram to deviations from estimated normal values that are compatible with both small pulmonary volumes and alveolocapillary block with arterial oxygen desaturation.

No known treatment exists for this disease. Steroids have been thought to be of value in some instances, but they have had no influence in most patients.

The exact nature of the PAS-positive material that fills the alveoli remains obscure, and the term "proteinosis" may be a misnomer for this disease. Payseur and associates[3] suggested that it is a mucoprotein, yet Lull and co-workers[4] found that it contained large amounts of nucleic acids and amino acids without true protein. An astonishingly high content of lipids, ranging up to six times the amount (dry weight) in normal lung tissue, has been reported.[1] There is a need for chemical analysis of fresh lung tissue to characterize the nature of this unusual intra-alveolar material accurately.

In view of the fact that the original report of this entity was presented only a little more than one year prior to the time of writing, one might wonder whether this disease has gone unnoticed among the multitude of other diffuse pulmonary diseases, perhaps as a variant of one of them, or whether this is a new disease process that is only now being encountered.

A number of theories regarding its pathogenesis have been proposed. Considerable interest has been displayed in the possible relationship between this disease and Pneumocystis pneumonitis. In disease caused by parasites of the genus Pneumocystis, the alveoli are filled with a foamy eosinophilic material that is also PAS positive. The lungs of these patients have an interstitial infiltration with plasma cells, and they lack the desquamation and degeneration of proliferating septal cells so characteristically seen in alveolar proteinosis. Structures considered to be cysts of the parasite classed Pneumocystis carinii can be demonstrated by Gomori's methenamine-silver nitrate technique.[5] Other distinct differences between these two diseases have been pointed out. Pneumocystis pneumonitis has been reported infrequently in the United States and has been seen predominantly in the lungs of infants dying in the first few months of life. The few adults with Pneumocystis pneumonitis usually have had an underlying debilitating disease, such as lymphoma or leukemia, which has not been a finding in cases of alveolar proteinosis.[5] It has been stated, however, that Plenk and associates[6] obtained a positive serologic reaction for Pneumocystis with serum from one of their patients who had alveolar proteinosis. This finding probably will renew the search for transitional forms between these two diseases, although the accuracy of this test has not yet been established.

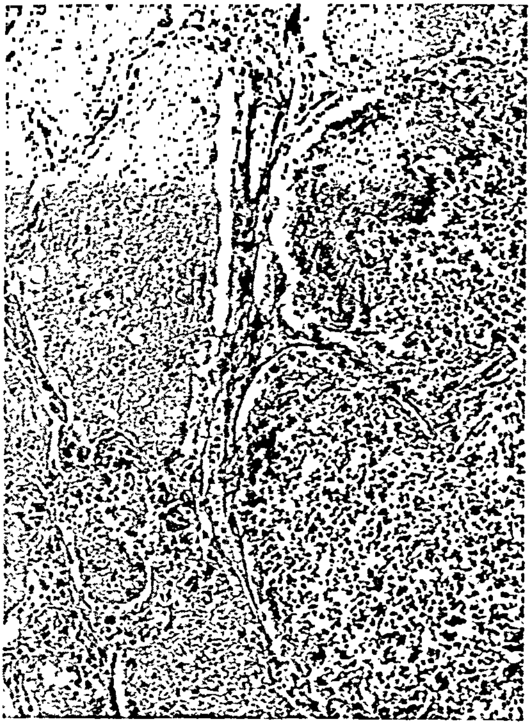
Fig. 4.—Superimposed focal pneumonitis: note lysis of amorphous material (PAS stain; × 100).

The possible role of occupational exposure, perhaps to a chemical inhalant, also has been considered in the pathogenesis of alveolar proteinosis. In six of the recorded instances of this disease, the patients worked with lumber, five in lumberyards and one as a carpenter. One patient in the series of Rosen and associates [1] had been exposed to various fruit and vegetable sprays; although our patient was a fruit wholesaler, no history of active exposure to such agents was elicited. Rosen's group also speculated that this disease may be "a penalty for the convenience of modern living," in view of the numerous aerosols, volatile solvents, and plastics to which these patients may have been exposed. They also mentioned that this may be a type of tissue reaction that can occur in response to more than one agent, in much the same way as a number of different disease processes are associated with the formation of a hyaline membrane in the lungs and even more with interstitial pulmonary fibrosis. The possibility that this disease could be the result of an immune response to a microbiological agent altered by recently developed antibiotics also has been suggested.[1] The premonitory febrile episode that preceded the development of dyspnea and usually was considered pneumonia in some of the reported cases suggests this possibility. One also wonders whether the characteristic lack of an inflammatory reaction to this amorphous material, unless a superimposed bacterial infection also is present, may not be a factor in its accumulation in the alveoli.

The prognosis in alveolar proteinosis has not been favorable. Including our patient, 9 of the 32 patients known to have alveolar proteinosis have died from progressive pulmonary insufficiency. In most patients, the disease has tended to follow a chronic course; the longest reported survival to date among the patients living at the last report has been 58 months. The average duration from the onset of the disease to death has been 11 months, and cyanosis was an early feature in all of the patients who died. The condition of seven patients improved, and the pulmonary infiltration apparently resolved in one of the patients reported on by Rosen and associates.[1] Fifteen patients have persisting pulmonary disease, with symptoms of varying intensity. Thus, the ultimate fate of a patient with alveolar proteinosis will remain uncertain until more knowledge is gained about its pathogenesis and a more successful mode of treatment is evolved.

Summary

A 42-year-old man, whose case is reported, had rapidly fatal pulmonary alveolar proteinosis. The clinical course was characterized by progressive pulmonary insufficiency, with secondary polycythemia and cor pulmonale. This is the ninth death in the 32 cases of alveolar proteinosis available for review.

Pulmonary alveolar proteinosis is a disease of unknown cause, with characteristic pathological changes in the lungs and a clinical course that may run independently of the extensive roentgenographic changes; it may be chronic or proceed to death in a few months from increasing pulmonary insufficiency. There is no known treatment.

Dr. Robert Bonifaci, Wenatchee, Wash., supplied the lung tissue used in this study for examination.

Addendum

Since completion of this manuscript, three additional nonfatal cases of pulmonary alveolar proteinosis have been reported.[7]

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NEWER CONCEPTS OF ARTERIOVASCULAR DISEASE.—One of the most important changes that has taken place in medicine is the concept that we should no longer look upon disease of the coronory arteries as a manifestation of heart disease, or strokes as a manifestation of brain disease, or senile diabetes as a manifestation of pancreatic disease, but that we should look upon most of these disorders as chance manifestations of a generalized process of atherosclerosis. . . .

If we think in terms of the changed concept, we should consider the matter as primarily one of atherosclerosis plus clotting. This point of view carries broad implications, much different than those involved in regarding a disease as merely capable of damaging a single organ. What we treat in the heart or brain is the end-result or by-product of a process that is more fundamental and biologically widespread.—I. S. Wright, M.D., Coronary Artery Disease: Progress and Problems, *Journal of the American Geriatrics Society*, April, 1960.

VACCINATION AGAINST RABIES WITH DUCK-EMBRYO AND SEMPLE VACCINES

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A comparison was made of the general and local reactions and the antibody titers produced in 123 patients given injection of duck-embryo rabies vaccine and 127 patients given brain–tissue rabies vaccine (Semple). The results indicate that duck-embryo rabies vaccine stimulates an earlier production of antibodies than Semple vaccine and that the range of antibody titers between the 11th and 15th days is not significantly different. Booster effects were obtained readily with both vaccines. In this study the complication of encephalomyelitis did not occur after the use of the duck-embryo vaccine but did occur in two patients who received the vaccine containing brain tissue. The recommendation that duck-embryo vaccine supplant the use of brain-tissue vaccine for prophylaxis of rabies seems to be justified.

Rabies vaccine has been used prophylactically, in human beings bitten by rabid animals, since the days of Pasteur. The amount of protection obtained varies, depending on the type of biting animal, location of bite, extent of injury, degree of protection by clothing, and other factors. All workers in the field agree, however, that the vaccine has definite protective value. This has been especially true since the establishment of standard techniques.[1] In recent years antiserum has been used together with vaccine for best results.[2]

The type of vaccine used most extensively in man is a suspension of rabbit brain which has been infected with fixed rabies virus. In some of the vaccines the virus has been inactivated; in others, it has not. Neither multiplies in the human being,[2c] however, so that for all practical purposes all antirabies vaccine used in man is dead vaccine. Inactivation is brought about by the addition of phenol or by exposure to ultraviolet light. Semple vaccine is of the former type and is one of the most popular in the United States. It is injected subcutaneously in a dose of either 2.0 ml. of a 5% suspension in saline solution or of 0.5 ml. of a 20% suspension.

One of the greatest drawbacks to the use of rabies brain–tissue vaccine is the occurrence of neurological complications after its use. Such accidents occurred in 44 persons treated in the antirabies clinics of the New York City Department of Health from 1928 to 1951.[3] They are believed to be due to sensitization to nerve tissue and have been produced in experimental animals.[4] Antibrain antibodies have been demonstrated in animals injected with brain substance[5] and in man receiving antirabies vaccine.[6] The advantage of a potent rabies vaccine free of brain tissue is obvious. Such a vaccine has been prepared in embryonated duck eggs infected with fixed virus, to which betapropiolactone 1:4,000 has been added.[7] It has been approved for use in human beings by the National Institutes of Health. Theoretically, such a vaccine should cause no neurological symptoms since it contains little or no brain tissue. In tests in guinea pigs no neuroparalytic factors could be demonstrated.[8] The development of antibodies against rabies in man by the 10th day after the first injection has been reported.[9]

The present investigation was undertaken to test the comparative routine prophylactic values of brain vaccine (Semple) and duck-embryo vaccine in patients in the antirabies clinics of the New York City Department of Health. About 400 persons a year receive such treatment in accordance with the recommendations of the World Health Organization's Expert Committee on Rabies.[10] The study was begun in July, 1957, and completed at the end of May, 1959. It was limited to the reactions caused by the administration of the two vaccines and the comparative abilities of the vaccines to stimulate the development of neutralizing antibodies.

Method of Study

Two antirabies clinics of the Department of Health, one in Manhattan and the other in Brooklyn, were used in this study. In each clinic a bound book was kept, in which successive lines were numbered from 1 to 200. Each new registrant's name was entered in the book in rotation. All persons with odd numbers received 14 daily injections of Semple vaccine; those with even numbers received an equal number of injections of duck-embryo vaccine. Injections were given subcutaneously, usually in the arm, in a dose of 0.5 ml. of Semple vaccine

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From the bureaus of preventable diseases and records and statistics, New York City Department of Health.

(20% suspension) or 1.0 ml. of duck-embryo vaccine. A chart was made out for each treated person and given a number corresponding to the one in the book. On the chart were entered the name, age, sex, color, and address of the vaccinee and the type of vaccine used. The chart also had spaces to indicate the dates when blood was drawn, when vaccine was administered, and the general and local reactions sustained after each injection. These were graded from 1+ to 4+. General reactions specifically inquired about were fever, malaise, nausea, vomiting, and muscle aches; local reactions listed were pain, swelling, redness, and abcess formation. At each visit inquiry was made about reactions to the previous injection.

A blood specimen was requested from each treated person prior to the first injection, again on the 10th, 15th, and 21st days, and again one month after completion of treatment. As many vaccinees as possible were recalled six to nine months after completion of treatment. A blood specimen was again obtained, a booster dose given, and another blood specimen obtained some weeks later. The blood specimens were delivered to the department's laboratory within a few hours and the serum was separated from the cells, drawn off into another sterile tube, and frozen in a deep freeze. About once a month the accumulated tubes were shipped by air express to Indianapolis for antibody determination. The tubes were labeled with the vaccinee's name and the date when the blood was obtained, but there was no notation about the type of vaccine used.

TABLE 1.—*Neutralizing Antibody Titers in Serums of Persons Injected with Duck-Embryo and Semple Rabies Vaccines*

Reciprocals of Antibody Titer Level	Specified Days After First Injection: 7-10 Days*		11-15 Days†		31-60 Days		6-9 Months‡	
	Duck	Semple	Duck	Semple	Duck	Semple	Duck	Semple
	No. of Serums Obtained							
0..........	22	51	14	13	5	2	4	5
4-15.9	40	22	35	24	17	5	9	13
16-63.9	18	4	40	39	35	24	21	16
64-127.9	2	0	7	10	12	24	2	5
128 and over	1	2	1	4	6	17	2	5
Total ...	83	79	97	90	75	72	38	44
	Percentage Distribution							
0..........	26.5	64.6	14.4	14.5	6.7	2.8	10.5	11.4
4-15.9	48.2	27.8	36.1	26.7	22.6	7.0	23.7	29.5
16-63.9	21.7	5.1	41.3	43.3	46.7	33.3	55.2	36.3
64-127.9	2.4	...	7.2	11.1	16.0	33.3	5.3	11.4
128 and over	1.2	2.5	1.0	4.4	8.0	23.6	5.3	11.4
Total ...	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0

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* About 90% of blood specimens were taken 9 or 10 days after the first injection; about 5% each were obtained 7 and 8 days after the first injection.

† About 75% of blood specimens were taken 13 or 14 days after the first injection; the rest were taken 11, 12, or 15 days after the first injection.

‡ Includes four blood specimens taken from 10 to 17 months after the first injection.

Results

During the period of study, 297 persons began treatment in the two clinics. Of these, 229 completed the series of 14 injections; the rest received from 1 to 13 injections. The distribution of 250 persons who received from 9 to 14 injections was as follows. There were more men than women (182 and 68) and more white than nonwhite persons (153 and 97) respectively. About equal numbers received Semple and duck-embryo vaccine (127 and 123), and in each age group (0-9, 10-19, 20-39, and 40 years of age or older) the distribution by type of vaccine administered and by age, sex, and color was similar. General reactions occurred in two persons only, both of whom received Semple vaccine; their cases are given below.

CASE 1.—A 47-year-old man received 14 injections of Semple vaccine. On the last day he complained of weakness, headache, and vomiting after the injection. His temperature rose to 102 F (38.9 C). Two days later he developed urinary retention and was admitted to a hospital. He had weakness in the lower extremities, diminished vibratory sensation, and a Babinski reflex on both sides. The white blood cell count was 16,400 per cubic millimeter, with a differential count of 78% polymorphonuclear cells. Spinal fluid cell count was 25 (5 polymorphonuclear cells and 20 lymphocytes) per cubic milliliter. A diagnosis of encephalomyelitis was made. The patient recovered.

CASE 2.—A 35-year-old woman received eight injections of Semple vaccine. After the last injection she had considerable local reaction, abdominal cramps, and weakness of both legs. Three days later she was admitted to a hospital with a temperature of 101 F (38.3 C), headache, and moderate nuchal rigidity. The white blood cell count was 8,900 per cubic millimeter, with 71% polymorphonuclear cells. The spinal tap yielded fluid with 82 cells per cubic milliliter, of which 98% were lymphocytes; the protein concentration was 103 mg. per 100 ml. The diagnosis was encephalomyelitis. Recovery was complete.

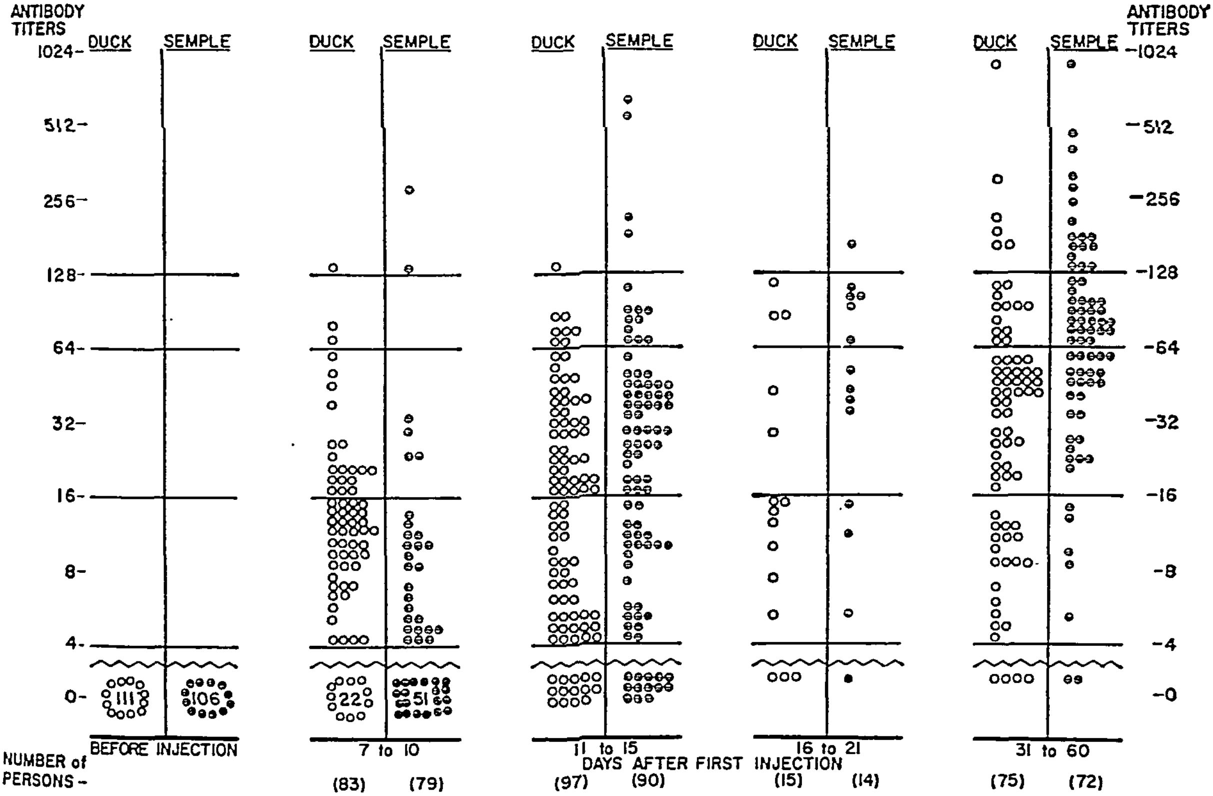
Local reactions according to grade were about the same after receipt of the two types of vaccine, although the severer reactions were somewhat greater after injection with Semple vaccine (3+ reactions occurring in only five subjects with use of duck-embryo vaccine versus nine with Semple vaccine, and no 4+ reaction occurring with use of duck-embryo vaccine versus one with Semple vaccine).

Laboratory Studies

Method of Antibody Titration.—The serum specimens were subjected to standard serum virus neutralization tests with use of white mice. Serums were inactivated at 56 C (132.8 F) for 30 minutes. Doubling dilutions of serum were mixed with equal volumes of a constant dilution of CVS strain of fixed rabies virus. Serum-virus mixtures were allowed to stand for one hour at 37 C (98.6 F) prior to injection. Six mice were used for each serum dilution level. A mixture of 0.03 ml. of serum-virus, containing 100 LD_{50}, was injected intracerebrally into each mouse, and the mice were observed for 14 days. Death and survival figures were calculated according to the method of Reed and Muench.[11] Antibody titers are expressed as the reciprocal of the serum dilution saving one-half the mice.

Serum Neutralizing Antibodies After Primary Immunization.—Pretreatment samples of blood serum were obtained from most subjects receiving vaccine. Only those from whom at least a second specimen was obtained are considered in the evaluation. Of these, 111 were injected with duck-embryo vaccine and 106 with Semple vaccine. None of them had antibodies to rabies virus before the injections were started. There were, in addition, nine persons who had antibody titers to rabies virus; they will be discussed later. It will be seen from table 1 and the figure that there was a more rapid rise in antibodies after injections of duck-embryo than of Semple vaccine. By the 10th day (see footnote 1, table 1), all but 26.5% of those receiving duck-embryo vaccine had neutralizing antibodies of 1:4 or higher, while 64.6% of those receiving Semple vaccine had no neutralizing antibodies. By the 15th day (see footnote 2, table 1), all but about 15% of both groups had measurable antibodies. Between one and two months after the first injection the rate of immunization was 93% for those who received duck-embryo vaccine and 97% for those who received Semple vaccine. By six to nine months after the first injection, measurable antibodies had dropped to about 88% in both groups.

A calculation of the median and the geometric mean of antibody titers showed again that the rise was more rapid and at a higher level up to the 10th day in those vaccinees receiving duck-embryo vaccine. Thereafter, the median and the geometric mean titers continued at a higher level in those receiving Semple vaccine (median, about 1:75 for Semple and about 1:40 for duck-embryo vaccine; mean, about 1:65 for Semple and about 1:30 for duck-embryo vaccine).



Distribution of antibody titers at stated intervals after first injection of duck-embryo and Semple vaccines.

Serum Neutralizing Titers After Booster Dose.—The 63 vaccinees who returned about seven months after the primary series of injections were given a booster dose of the vaccine they had originally received, immediately after a blood specimen was taken. A postbooster blood specimen was requested several weeks later. All responded to the booster dose, even those who had no measurable antibodies prior to the injection. The titers for both types of vaccine, in general, reached much higher levels than after the primary series of injections (a mean of 1:390 [Semple] and of 1:230 [duck-embryo] after the booster dose compared to about 1:20 for both types after primary doses).

The preinoculation serum specimens of nine persons had had neutralizing antibodies in titers of 1:4 to 1:41 before the present series of injections was begun. Six had received a full series of 14 injections of Semple vaccine 2 to 17 years previously. The other three denied having received anti-rabies injections previously. It will be noted in table 2 that a booster effect was obtained in those previously inoculated, irrespective of whether the vaccine used in the present series was duck embryo or Semple. No such booster effect was noted in the three vaccinees who denied having received rabies vaccine previously.

Table 2.—*Serum Antibody Response in Persons Receiving Rabies Vaccine Who Had Preinjection Titers of Neutralizing Antibodies to Rabies Virus*

Case No.	No. of and Interval, Yr., Since Previous Injections of Vaccine		Antibody Titers on Indicated Days After 1st Injection				Type of Vaccine
	No.*	Yr.	Preinjection	7-10	11-15	31-60	
1	14 14	10 7	10.3	>610.0	680.0	20	Semple
2	14	7	30.0	670.0	1,350.0	105	Semple
3	5	2	11.2	34.0	>170.0	800	Duck
4	3 series of 14	12-17	41.0	1,180.0	1,220.0	180	Duck
5	14	14	4.0	380.0	780.0	...	Duck
6	14	3	17.8	3,700.0	4,090.0	1,170	Duck
7	...	...	4.7	42.0	610.0	...	Duck
8	...	...	4.5	12.3	17.4	...	Semple
9	...	...	27.0	21.0	16.0	8	Duck

* One series=14 injections.

Six veterinarians on the staff of the Department of Health, who had received one or more series of Semple vaccine in previous years, were given a single injection of duck-embryo or Semple vaccine after a specimen of blood had been drawn. Two to four weeks later another blood specimen was obtained. The prebooster and postbooster antibody responses are given in table 3. It will be noted that only two of these six subjects had no measurable antibody in their blood serum, prior to the booster dose. All responded with a good titer to a booster dose, even one (case 3, table 3) who had received only three or four injections 19 years previously. Good responses were obtained whether the booster dose was duck-embryo or Semple vaccine.

Comment

This investigation was undertaken to test the effectiveness of duck-embryo killed rabies vaccine in the prophylaxis of rabies. The need for such a vaccine is mainly due to the fact that the vaccines in common use today contain brain tissue, which causes encephalomyelitis in a certain percentage of persons injected. While this percentage has been reported to be low in most investigations,[3] one group reported it to be as high as 1 in 600 treatments.[12]

The rarity of human rabies in New York City made a field study impracticable. The present study was limited, therefore, to a comparison of general and local reactions and of antibody titers after injections of a duck-embryo vaccine and a brain-tissue vaccine (Semple). There was no significant difference in local reactions between the two. Two cases of encephalomyelitis occurred among the Semple-treated group.

Tests for rabies neutralizing antibodies were made on all blood specimens received. They developed sooner after injection of duck-embryo than of Semple vaccine. By the 10th day after the first injection, 74% of recipients of the former and 35% of the latter had developed neutralizing antibodies in a titer of 1:4 or higher. By the 15th day, about 86% in both groups had measurable antibody, and about one month after the first injection 93 and 97%, respectively, had developed antibodies. The median and geometric mean titers were significantly higher in those treated with duck-embryo vaccine before the 11th day after the first injection and higher in the Semple-treated group thereafter. The difference between the two groups in the 11-to-15-day period was not statistically significant.

Only nine persons had neutralizing antibodies in their blood prior to the start of treatment. Six of them had a booster antibody response after the injection of vaccine. These persons had received Semple vaccine from 2 to 17 years previously. Six veterinarians, who had received injections of Semple vaccine previously, were given a single dose of duck-embryo or Semple vaccine. Four of the six had prebooster antibody titers; all responded with a booster type of increase in titer, even the two who had had no measurable antibody titer in their blood prior to the booster dose. One of the veterinarians had received several series of Semple vaccine 20 years previously. Of particular interest are two of the veterinarians. One had received only three or four injections of Semple vaccine 19 years previously. He had a serum titer of zero prior to the

Table 3.—*Serum Antibody Response to Booster Dose in Veterinarians Who Had Previously Received Semple Vaccine*

Case No.	No. of and Interval, Yr., Since Previous Injections of Vaccine		Neutralizing Antibody Titer		Type of Booster Vaccine
	No.	Yr.	Prebooster	Postbooster	
1	7	14	0.0	23	Semple
2	14 14	15 13	28.0	870	Semple
3	3-4	19	0.0	555	Semple
4	14 14	20 15	9.9	72	Duck
5	21 14 14	21 20 20½	97.0	370	Duck
6	14	16	4.0	195	Duck

booster dose and one of 1:555 after the booster. The other had received seven injections of Semple vaccine 14 years previously. After a booster dose he had an antibody titer of 1:23. Apparently, previous treatment conditions the recipient to respond to a booster dose, even though the original treatment was given many years previously. This was also demonstrated by Fox and co-workers.[13]

The data presented indicate that duck-embryo rabies vaccine stimulates an earlier production of antibodies than Semple vaccine and that the range of antibody titers between the 11th and 15th days is not significantly different after the use of either. Booster effects are obtained readily with both vaccines. Since there is reason to believe that the complication of encephalomyelitis does not occur after the use of the duck-embryo vaccine but does occur in some persons after the use of vaccines containing brain tissue, the recommendation that duck-embryo vaccine supplant the use of brain-tissue vaccine for prophylaxis of rabies seems to be justified.

Summary and Conclusions

Duck-embryo killed rabies vaccine was compared with Semple rabies vaccine in the prophylaxis of rabies. Local reactions occurred to about the same extent in groups of patients treated with each. Two cases of encephalomyelitis occurred in the Semple-treated group. Serum antibody titers began to rise sooner in those treated with duck-embryo vaccine; by the 10th day 74% of these had a titer of 1:4 or higher, in contrast with 35% of those treated with Semple vaccine. By the 15th day 86% of both groups had developed measurable antibodies, and about one month after the first injection about 95% had measurable antibodies.

A booster dose, given six to nine months after the beginning of treatment, evoked a booster response, with titers higher than those reached after the primary series. Four persons who had received one or more series of injections as long as 20 years prior to the study still had circulating antibodies in their blood and responded with a booster effect after a single injection. The earlier development of antibodies and the absence of the complication of encephalomyelitis after the use of duck-embryo vaccine suggests its use in the prophylaxis of rabies in preference to vaccines containing brain tissue.

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The vaccines used in this study were supplied by Dr. F. B. Peck Jr., of Eli Lilly and Company, Indianapolis 6.

Drs. Samuel A. Cohen, Louis Levin, and Jeanne Shore administered the vaccine injections and obtained the blood specimens. Horace M. Powell, Sc.D., performed the titrations.

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J.A.M.A., May 28, 1960

HODGKIN'S DISEASE WITH INVOLVEMENT OF THE HEART AND PERICARDIUM

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The heart was found to be involved in 3 of 15 cases of Hodgkin's disease. In one patient, a 46-year-old man, the myocardium showed a striking degree of fibrosis, with nodules of cells exhibiting extreme pleomorphism and a tumor mass protruding into the cavity of the right atrium. In the second patient, a 68-year-old woman, an infiltrate of lymphocytes, macrophages, and Reed-Sternberg cells was found in both myocardium and epicardium. In the third patient, a 50-year-old man, two nodules on the epicardial surface revealed massive infiltration of the subepicardial tissue with large pleomorphic cells, multinucleated giant cells, typical Reed-Sternberg cells, and nests of lymphocytes. In each case the history contained some evidence of cardiac disturbance. Unexplained arrhythmias and decompensation refractory to the usual treatment are two common manifestations of myocardial metastases.

An autopsy on a patient with Hodgkin's disease, with cardiac involvement, prompted us to review the literature on this relatively rare manifestation. This case and two others taken from our files will be reported. Although reference will be made to the general subject of cardiac metastasis from malignant tumors, this communication will deal mainly with detailed reports of cases of Hodgkin's disease with cardiac involvement. In this discussion tumors of the pericardium will be considered along with those of the heart proper.

Review of Literature

The recent literature indicates that the heart is rarely involved by Hodgkin's disease. The classic review by Jackson and Parker [1] cited 63 autopsies in cases of Hodgkin's granuloma. Of these, only two showed pericardial tumor. Several additional cases showed pericardial effusion, but there were no tumor nodules present in the pericardium or epicardium. In none of the authors' 98 autopsies in cases of Hodgkin's disease, including paragranuloma, granuloma, and sarcoma, was there myocardial involvement.

In 1939 Harrell [2] reported eight recorded cases of Hodgkin's disease with pericardial involvement and added a ninth case. Ritvo [3] reported a case of Hodgkin's disease in which the patient survived 17 years after diagnosis. At autopsy extensive invasion of both heart and pericardium was seen. The unusually long survival time was attributed to an excellent response to x-radiation therapy. In 1941 Garvin [4] cited a case of Hodgkin's disease with extensive involvement of the heart and pericardium. This was apparently the first report of ante mortem diagnosis of Hodgkin's disease with cardiac involvement. Hagans [5] in 1950 reported an unusual case of Hodgkin's disease which initially presented signs and symptoms of pericarditis with effusion. De Loach and Haynes [6] in 1953 reported 3 cases of cardiac involvement in 49 cases of Hodgkin's disease. In two of these there was involvement of the myocardium and in one of the pericardium. Bisel and co-workers [7] noted 8 cases of cardiac involvement in 31 cases of Hodgkin's disease. The exact site of involvement, with respect to pericardium, epicardium, or myocardium, was not stated. Also, in the same year, Nabarro [8] reported 24 cases of Hodgkin's disease, 4 of which showed both gross and microscopic involvement of the heart. One showed only microscopic involvement. Rottino and Hoffman [9] cited five additional cases. In four of these, however, the lesions were small and apparently insignificant, affecting only the visceral or parietal pericardium. Their fifth case demonstrated involvement of the right auricle with obstruction of the inferior vena cava and tricuspid orifice.

Report of Cases

In our own series of 15 cases of Hodgkin's disease, cardiac involvement was noted in 3. One case showed involvement of the myocardium, one of the epicardium, and a third of both epicardium and myocardium.

Case 1.—This patient had Hodgkin's disease, with obliteration of the pericardial sac and widespread involvement of the myocardium, mediastinal structures, lymph nodes, spleen, and other viscera. A 46-year-old man was first admitted to Mount Sinai Hospital in August, 1956, for evaluation of a mass in the chest discovered on routine x-ray examination. On Aug. 8, 1956, a left-sided thoracotomy was performed, with incomplete resection of an anterior

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mediastinal mass which had invaded the pericardial sac. Pathological examination established the diagnosis of Hodgkin's disease. In 1957 the patient was readmitted to Mount Sinai Hospital with clinical evidence of obstruction of the superior vena cava. In 1958, he manifested weakness and atrophy of the lower extremities, suggesting cord involvement. In each instance satisfactory clinical improvement was obtained as a result of a course of nitrogen mustard and x-radiation therapy. In January, 1959, he developed atrial flutter with variable degrees of heart block (fig. 1). The arrhythmia could be well controlled with digitalis, but it was interpreted as due to myocardial involvement with Hodgkin's disease. His final admission was on March 14, 1959, because of marked weakness and profound anemia.

Physical examination revealed a chronically ill patient in no acute distress. Examination of the neck showed enlarged, firm lymph nodes in the left supraclavicular fossa. The lungs were resonant. A few fine rales were noted at the left lung base. A faintly audible pericardial friction rub was present over the precordial area. There were no other remarkable cardiac findings. The liver edge was 2 fingerbreadths below the right costal margin but nontender. The spleen and kidneys could not be palpated.

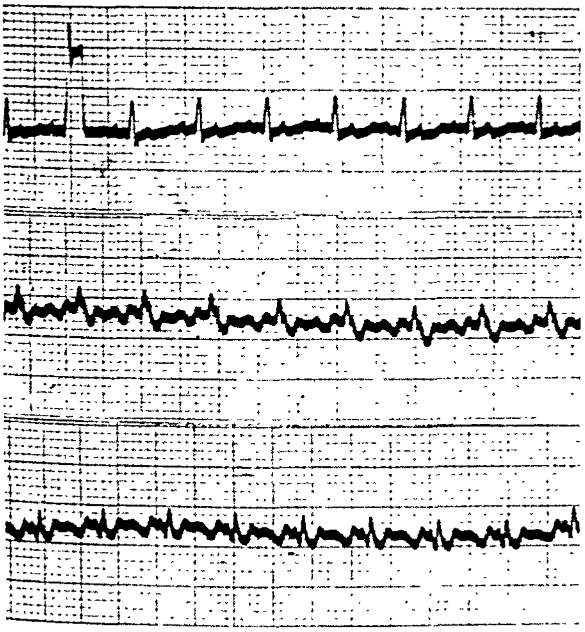

Fig. 1 (case 1).—Standard leads, showing atrial flutter with 2:1 block.

After admission, a routine blood count showed a hemoglobin level of 7.7 Gm.% and a hematocrit reading of 29%. A roentgenogram of the chest showed a density of the left lung area considered to represent pleural and parenchymal involvement with Hodgkin's disease. Electrocardiogram showed normal rhythm with slight S-T segment and T wave changes. Treatment was mainly symptomatic, including administration of antibiotics and digitalis and blood transfusions. During the last transfusion, on March 20, 1959, the patient developed intractable pulmonary edema and died several hours later.

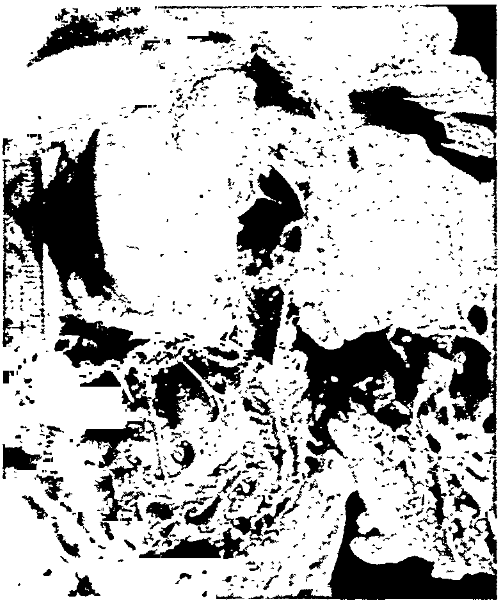

Fig. 2 (case 1).—Photograph of tumor in right atrium arising from endocardial surface above tricuspid valve.

Autopsy Findings.—The pleural cavities each contained about 1,000 cc. of fluid. The left lung was firmly adherent to the chest wall, laterally and posteriorly, by means of thick fibrous adhesions. Medially, the left lobe was plastered against the chest wall by thick, firm, yellow tumor tissue. The lungs showed severe edema. The pericardial sac could not be identified, evidently because of its removal as part of the tumor mass at previous surgery. The heart weighed 650 Gm. and showed a diffusely thickened epicardium.

The cavity of the right atrium was partially obliterated by a tumor measuring 6 cm. in diameter and arising from beneath the endocardial surface just above the anterior cusp of the tricuspid valve (fig. 2). On section, the tumor was shown to consist of firm, fleshy, gray tissue divided into lobules by thin white fibrous septums. The left ventricular myocardium was diffusely invaded by tumor tissue. A similar lesion was found in the interventricular septum. Sections from various tumor sites had a similar microscopic appearance. Sections of the heart revealed a striking picture of myocardial fibrosis as well as nodules of cells exhibiting extreme pleomorphism (fig. 3). The various cell types noted were rare lymphocytes, eosinophils, large mononuclear cells, and giant cells of the Reed-Sternberg type (fig. 4). Sections from the region of the tricuspid valve showed a tumor invading the myocardium as well as the subendocardial layer, with no involvement of the valve proper or endocardium.

Comment.—In this case, the development of cardiac arrhythmia, as recorded by electrocardiogram, was regarded as possibly indicating myocardial invasion by Hodgkin's disease.

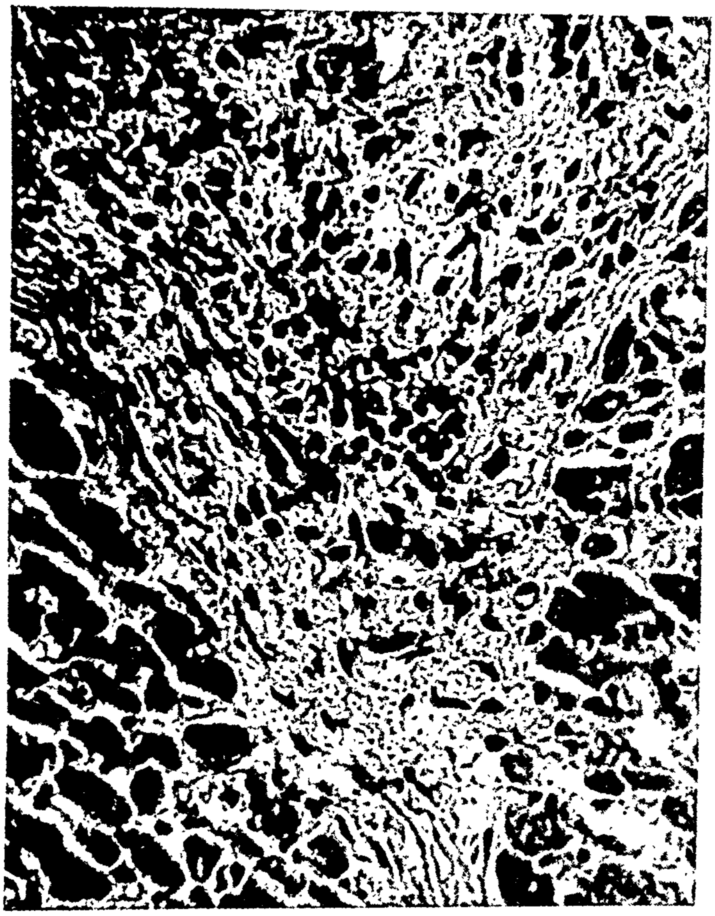

Fig. 3 (case 1).—Histological section of tumor, showing diffuse involvement of intraventricular septum (× 160).

CASE 2.—A 68-year-old woman was admitted to Mount Sinai Hospital on April 19, 1956, with the chief complaint of shortness of breath, epigastric pain, weakness, and persistent fever of six weeks' duration. These symptoms were associated with thrombophlebitis of the left lower extremity and a rapidly enlarging mass in the left upper quadrant believed to be spleen. Physical examination on admission revealed that the spleen extended 4 fingerbreadths below the left costal margin and the liver 5 fingerbreadths below the right costal margin. There was no significant lymphadenopathy. Laboratory findings included leukopenia, anemia of slight degree, and a positive result of the Kline test, in the absence of a history of syphilis. Roentgenograms of the chest, gastrointestinal series, barium enema examination, and intravenous pyelography were noncontributory. Marrow studies were not diagnostic and liver biopsy showed a slight portal hepatitis. The electrocardiogram demonstrated a nodal tachycardia.

The diagnosis of lymphoma was entertained, but abdominal exploration could not be carried out because of the patient's poor condition. She started on a course of x-ray therapy to the spleen, as well as administration of steroids, with a remarkable improvement in her general condition. The remission was short-lived, however, and chemotherapy with nitrogen mustard and triethylene-thiophosphoramide was initiated. Her condition deteriorated rapidly and she died two months after admission.

Autopsy Findings.—Each pleural cavity contained 200 cc. of clear yellow fluid. There was moderate bilateral pulmonary edema. The heart weighed 350 Gm. and was not remarkable on gross examination. Liver and spleen were both enlarged, the former weighing 2,250 Gm. and the latter 770 Gm. There was about 1,000 cc. of clear yellow fluid in the peritoneal cavity.

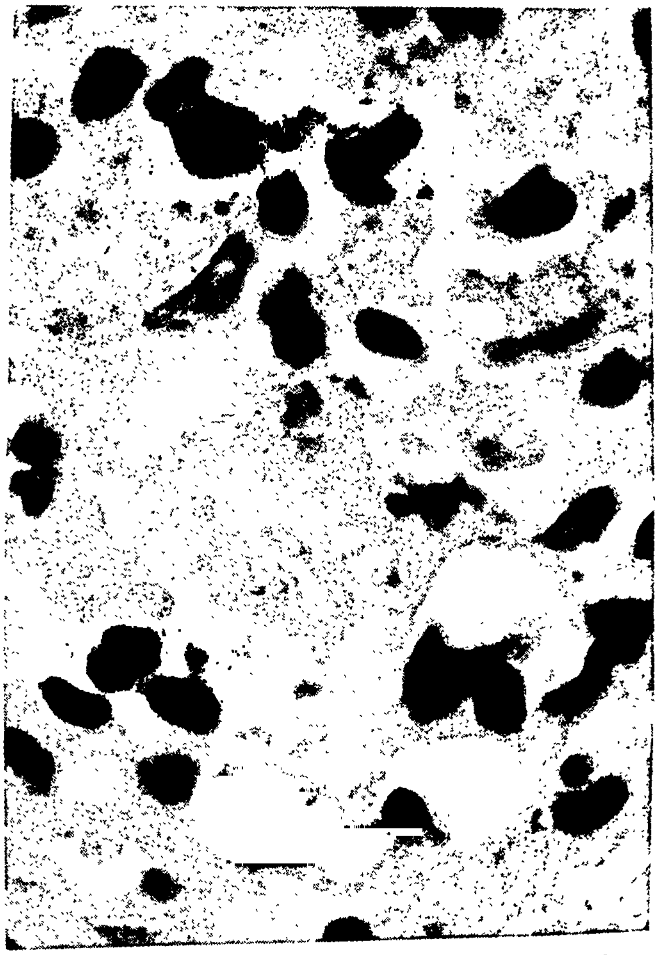

Fig. 4 (case 1).—High-power view of similar field, showing fibrocytes, mononuclear cells, and multinucleated giant cells of Reed-Sternberg type (× 440).

On microscopic examination, lesions of Hodgkin's disease were seen in the lymph nodes, liver, spleen, lungs, and other viscera. Sections of the myocardium showed an interstitial infiltrate consisting chiefly of lymphocytes, macrophages, and cells of the Reed-Sternberg type. A similar infiltrate was found in the epicardium; however, no pericardial involvement could be demonstrated.

Comment.—This case represents an acute disseminated variety of Hodgkin's disease with widespread visceral involvement. Myocardial involvement was not suspected ante mortem, since the electrocardiographic finding of a nodal tachycardia could also be explained on the basis of the patient's febrile course.

Case 3.—A 50-year-old man was first admitted to Mount Sinai Hospital on Oct. 26, 1952, with a four-week history of dull, aching pain over the left lower part of his chest associated with general malaise and weakness. A biopsy of a cervical node performed at another hospital nine years previous to this had demonstrated Hodgkin's disease. Subsequently the patient was treated with x-radiation and apparently remained in satisfactory condition until the present hospital admission.

Physical examination revealed a well-developed, well-nourished man, with a palpable left supraclavicular lymph node, a palpable liver, and deep tenderness to palpation in the left upper quadrant of the abdomen. Laboratory studies showed hypochromic anemia, negative urinary findings, and occult blood in the stools. Roentgenogram of the chest showed moderate cardiac enlargement and bilateral pulmonary infiltrate, probably representing tumor. X-ray examination of the spine showed no evidence of sclerosis or destruction of vertebrae. An upper gastrointestinal study demonstrated the presence of a fistulous tract between the stomach and the hilar area of the spleen, with a definite extravasation of barium between the two organs.

During the first and subsequent admissions to the hospital the patient was treated chiefly with x-radiation. This resulted in only slight clinical improvement. Because of severe low back pain, thought to be the result of cord involvement, a bilateral cordotomy was performed.

At the time of the fourth and last admission, on Jan. 30, 1953, the left supraclavicular mass had grown to the size of a small grapefruit. There was dulness, and breath sounds were absent, at the left lung base, indicating pleural effusion. There was marked tenderness over the right iliac crest and 4+ pitting edema of the lower extremities. It was the clinical impression that the inferior vena cava was being compressed by a large retroperitoneal tumor mass. The patient's condition deteriorated rapidly and, on Feb. 21, 1953, he developed Cheyne-Stokes respiration and became comatose. He died two days later, with terminal hyperpyrexia.

Autopsy Findings.—The left pleural cavity contained about 1,400 cc. of slightly turbid yellow fluid. The parietal pleura was markedly thickened and showed multiple firm light gray nodules. Both lungs contained similar multiple nodules. The peritoneal cavity contained no fluid. On the posterior wall of the stomach, along the greater curvature, there was a large ulcerated mass measuring 5 by 3 by 1 cm. A fistulous tract connected the gastric mass with the spleen. The heart weighed 285 Gm. and showed two firm light gray ovoid nodules on the epicardial surface. The pericardium was not involved.

Microscopic examination showed evidence of Hodgkin's disease in the lymph nodes, esophagus, stomach, spleen, lungs, liver, left adrenals, ribs, and 11th and 12th thoracic vertebrae. Section of one of the nodules in the epicardium revealed massive infiltration of the subepicardial fatty tissue with large pleomorphic cells and multinucleated giant cells. Typical Reed-Sternberg cells were present, as were nests of lymphocytes. The myocardium showed an increase of interstitial fibrous connective tissue, with patchy areas of fibrosis but no tumor.

Comment.—In this interesting case of Hodgkin's disease, with an associated gastrosplenic fistula, the presence of cardiac metastases was not suspected ante mortem.

Comment

Metastatic tumors of the heart and pericardium are usually a manifestation of advanced malignant disease. The primary lesion may be located in practically any organ; however lesions of the breast and lung, lymphoma, leukemia, and malignant melanoma are most frequently complicated by this condition. Various large autopsy series show a wide range of frequency of cardiac involvement.[10] Figures range from 1 to 21% of cases of malignant disease.

The embolic transfer of tumor cells from the primary site to the heart is supposed to be the most frequent mode of metastasis. Prichard [10b] and others have stated that the lymphatic route of spread is more frequent than spread by direct extension, even in cases of carcinoma of the lung and other extracardiac intrathoracic malignant processes. When direct extension does occur, its form may be unusual, with invasion of the pulmonary vein and extension into the left atrium or invasion of the superior vena cava and extension into the right atrium. Scott and Garvin [10c] cited embolic metastases via the coronary arteries as the most frequent mode of metastasis to the heart. They considered involvement by retrograde lymphatics less frequent than direct extension from the lungs or mediastinal nodes. In the special case of Hodgkin's disease and of malignant lymphoma one must also consider the possibility of a multicentric origin. Often one may not be able to point to a primary tumor, at best only a primary region of involvement. There is evidence that the abnormal growth stimulus which gave rise to the original primary tumor may subsequently affect distant sites, especially those containing relatively large amounts of lymphoid tissue. This may account for the relatively less frequent involvement of the heart as compared to the spleen, liver, and lymph nodes. Nevertheless, it has been found that the percentage of cardiac involvement in cases of lymphosarcoma and Hodgkin's disease is generally higher than in cases of carcinoma.

The nature of the cardiac involvement is variable. Metastatic carcinoma or sarcoma usually occurs as discrete nodules involving pericardium, epicardium, and myocardium, the former two sites being more common. Leukemic infiltration and secondary lymphoma are more commonly diffuse. Neoplastic lymphangitis has occurred. Rarely, the nodules in the myocardium develop into large tumor masses which seriously encroach on a cardiac chamber. The cardiac involvement is often associated with a fibrinous pericarditis. In rare instances parenchymal lesions are absent; however, miliary infarction of the myocardium occurs as a result of the tumor emboli in coronary vessels. Endocardial involvement is considered to be the most unusual form of metastasis. Coller, Inkley, and Moragues [11] reviewed the literature in 1950 and found only nine cases with endocardial involvement, six of which showed implantation on the tricuspid valve. They added a single case considered to be the first reported instance of mitral valve implantation and another case with combined mitral and aortic valve involvement. The rarity of valvular implants has been explained by Prichard [10b] on the basis of the relative avascularity of the endocardium. Coller and collaborators were of the opinion that the valvular implants could occur only in the presence of preexisting valvular disease.[6]

The presence of cardiac metastases can be entirely asymptomatic, without associated disturbance of cardiac function; therefore the diagnosis is difficult and is rarely made ante mortem. Pericardial involvement may be suggested by signs of cardiac tamponade, with cardiac decompensation; a rigid nonpulsating cardiac border on fluoroscopy; electrographic evidence of pericarditis; or a persistent or recurring pericardial effusion. The presence of tumor cells in pericardial fluid obtained by thoracentesis is diagnostic. On the other hand, absence of fluid does not rule out the diagnosis, since the entire pericardial cavity may be obliterated by tumor.

The most common clinical manifestation of myocardial involvement by tumor is unexplained cardiac decompensation entirely refractory to the usual treatment. This feature has been emphasized by several authors. Arrhythmias constitute the second most common manifestation of myocardial metastases, and these may include an unexplained sinus tachycardia, premature atrial and ventricular contractions, bundle-branch block, or complete heart block. Disturbances of rhythm are usually associated with atrial involvement, particularly of the right atrium. Occlusion of the coronary artery by tumor may give rise to symptoms of angina pectoris. Sudden death also may be associated with cardiac metastases.

Summary

Cardiac involvement is relatively rare in Hodgkin's disease, but its occurrence in 3 of 15 cases indicates that the incidence may be greater than formerly recognized. The degree of involvement varies considerably, from microscopic foci to massive tumor nodules which give rise to arrythmias and cardiac decompensation.

Dr. Harry Golblatt gave advice and criticism in the presentation of these findings. Miss Josephine Jones and Mrs. Frances Christovitch provided technical assistance. Mr. Robert Newhouse supplied the photographs. Misses Diane Tanner and Sandra Barnes assisted in the preparation of the manuscript.

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ENTRANCE OF BARIUM INTO INTESTINAL GLANDS DURING BARIUM ENEMA

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Evidence that barium sulfate, administered by enema as a contrast medium for roentgenologic study of the colon, actually enters the lumens of the intestinal glands was obtained in the case of a 24-year-old man. That this was not the result of individual peculiarities or of local disease was shown by further studies in five unselected female patients, for biopsy showed barium sulfate crystals within some of the intestinal glands after a barium enema in each case. It was also found that pathological changes followed. This suggests that in the production of barium granulomas the barium enters through the lumens of the intestinal glands.

There has been no mention in the literature of barium sulfate observed within the intestinal glands after a barium enema. This paper is presented primarily to demonstrate a case in which a barium enema showed what is believed to be filling of numerous intestinal glands; second, to present histological evidence that barium does enter the glands; and third, to demonstrate that it causes pathological changes within the glands and may therefore explain the portal of entry and the mechanism of some cases of barium granuloma occurring after barium enemas.

Report of Investigation

A 24-year-old hyposthenic man presented himself with clinical symptoms suggestive of a mild irritable colon syndrome and recent onset of hemorrhoids. Result of physical examination was normal. Proctosigmoidoscopy showed normal mucosa except for second-degree hemorrhoids. Barium enema examination, with use of a self-retaining balloon catheter showed no abnormalities. However, the postevacuation film showed numerous minute spicules of barium projecting at right angles from the margins of the transverse and descending colon (fig. 1). They were remarkable in that they were perpendicular to the contour of the colon and were uniform in shape and size, measuring about 0.5 to 0.8 mm. in length.

The outline of the colon between the spicules was sharply defined and smooth and showed no signs of irritability. These projections were too fine and uniform to be interpreted as prediverticula or ulcerative colitis. Other causes of contour irregularities such as mucus, fecal residue, and spasm were considered and discarded because of the appearance of the spicules. The interpretation was that this represented barium which had entered the lumens of some of the intestinal glands, rendering them radiopaque. Three weeks later a biopsy specimen (fig. 2) was taken from the mucosa of the second rectal valve to see if there were any histological peculiarities to explain the findings, and serial sections revealed no abnormalities. A barium enema examination was given nine months later, with the same type of barium medium (Gastropaque), and at this time the contour was smooth and without spicules.

Method of Investigation.—In order to determine whether or not barium can enter the lumens of the intestinal glands during barium enema examinations, the following investigation was carried out. Five unselected patients were given barium enemas for various indications, and immediately after the postevacuation films were taken, sigmoidoscopy was done, the residual barium was washed and wiped away from the edge of the second or third rectal valve, and a punch biopsy was taken. Serial sections were made of each and studied for the presence and location of barium sulfate crystals. Two different barium preparations were used to see if differences would be noted. To aid in the identification of the barium crystals, a piece of Gelfoam was saturated with barium and it was prepared by the routine paraffin method, sectioned, and studied (fig. 3) in the same manner as the biopsy specimens.

*Results of Rectal Biopsy in Five Unselected Patients**

Case No.	Age, Yr.	Diagnosis	Barium Preparation
1.................	59	Internal hemorrhoids	Gastropaque
2.................	65	Diverticulosis	Veri-O-Pake
3.................	41	Follow-up for polyp of colon	Veri-O-Pake
4.................	47	Irritable colon	Gastropaque
5.................	63	Irritable colon	Gastropaque

* All patients were female, and the presence of barium was noted in the glands of all.

Results.—It was found that the biopsies in each of the five cases showed barium sulfate crystals to be present within some of the intestinal glands (see table). There were no differences noted between the two barium preparations used. The barium sulfate crystals were pale yellow and either

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amorphous or in the shape of rhomboid plates of varying sizes. They were doubly refractile to polarized light, which facilitated their search.

It was also found that pathological changes occurred in association with the presence of barium sulfate crystals in the glands. Figure 4 demonstrates the case of one patient in whose glands barium sulfate crystals had entered the lumen and become deposited near the neck of the gland. In this area rupture of the cell membranes has occurred, with obliteration of the intercellular boundaries.

Comment

It is concluded that during barium enema examinations, barium enters the lumens of intestinal glands. These intestinal glands are stated to be 0.5 to 0.8 mm. long,[1] and this corresponds to the measurements of the spicular projections seen on the film (fig. 2). It is believed that the occasional isolated spicule seen along the contours of the colon in many barium enema examinations may be due to filling of an intestinal gland.

It is also concluded that intraglandular deposits of barium sulfate crystals injure the cells of the intestinal glands. It is proposed that this is the mechanism by which barium granulomas form after barium enemas have been given. There are four cases reported by Gordon and Clyman[2] and

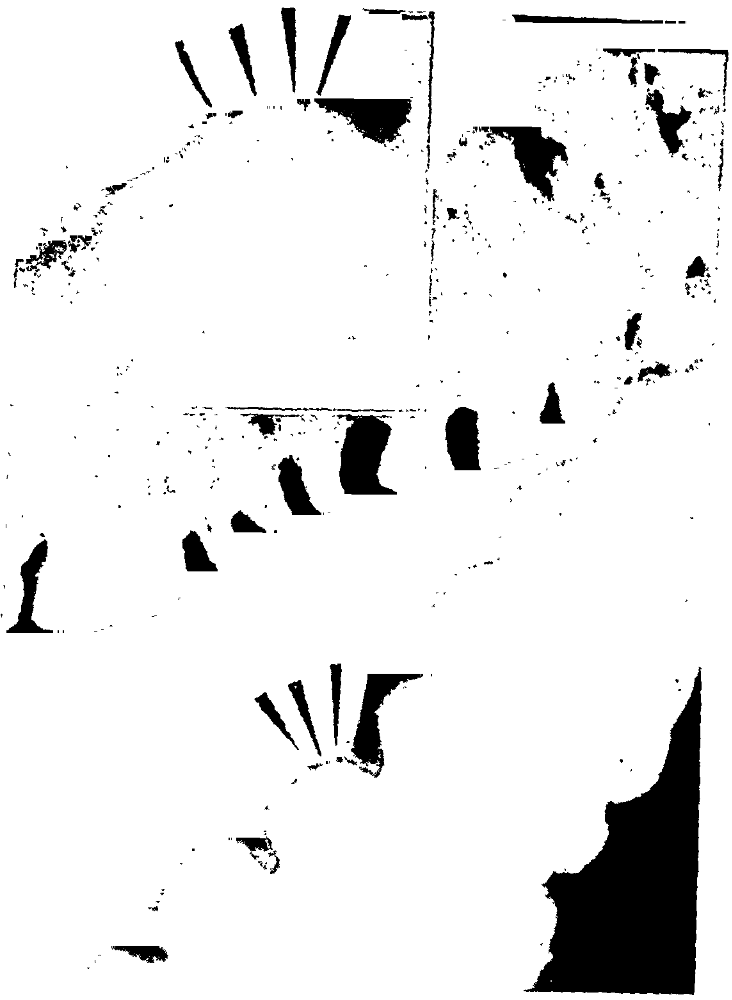

Fig. 1.—Postevacuation film, showing fine spicules of barium arising from contour of transverse and descending colon. *Arrows* point to 4 spicules, 11 of which were counted on medial aspect of this particular haustrum. Note spicules present on other haustra. *Inset:* haustrum enlarged two and one-half times.

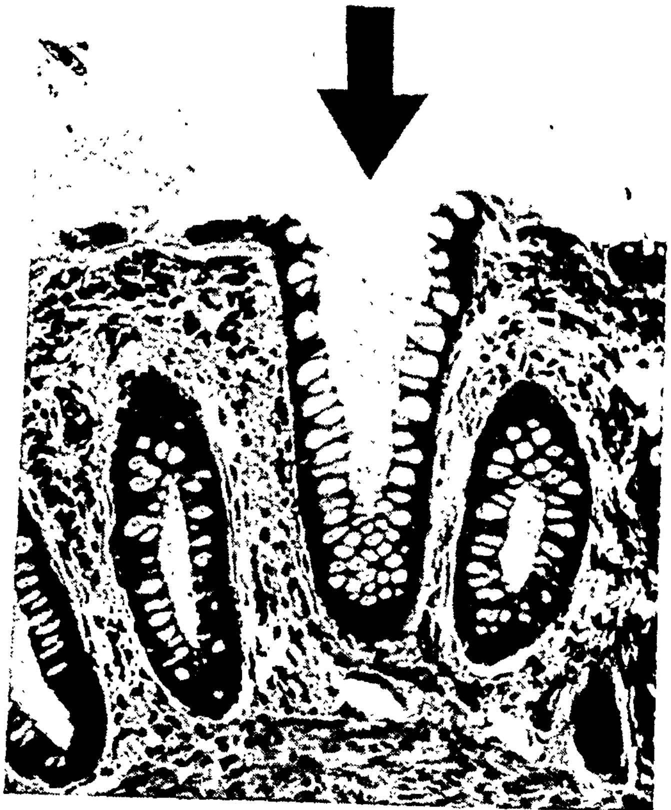

Fig. 2.—Rectal biopsy specimen from same case as shown in figure 1, showing normal intestinal glands. Note opening of gland through which barium can enter (× 150).

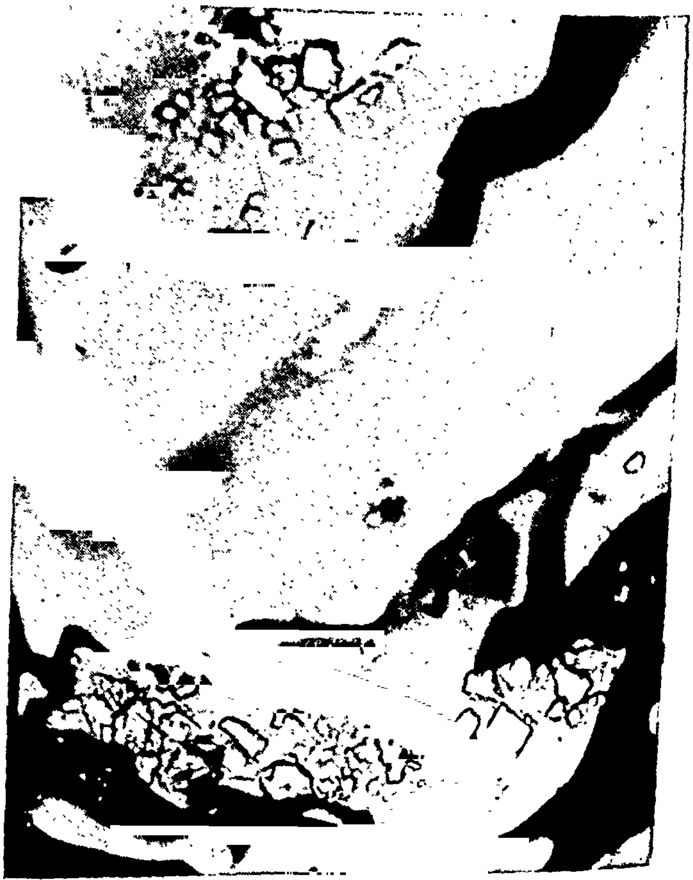

Fig. 3.—Barium sulfate crystals in Gelfoam, photographed in polarized light (× 540).

one by Beddoe and co-workers,[3] in which barium granulomas of the submucosa of the rectum were found or removed 2 to 25 days after barium enema examinations. They were all small, measuring 3 to 10 mm. It was suggested by the authors that the rectal mucosa may have been traumatized during the barium enema examination, allowing the barium to enter the submucosa, with subsequent development of a foreign body granuloma. However, in four of five cases the mucosa was intact over the lesion, and in the fifth there was a microscopic ulceration of the mucosa which may have been secondary to the underlying granuloma rather than being the traumatic point of entry.

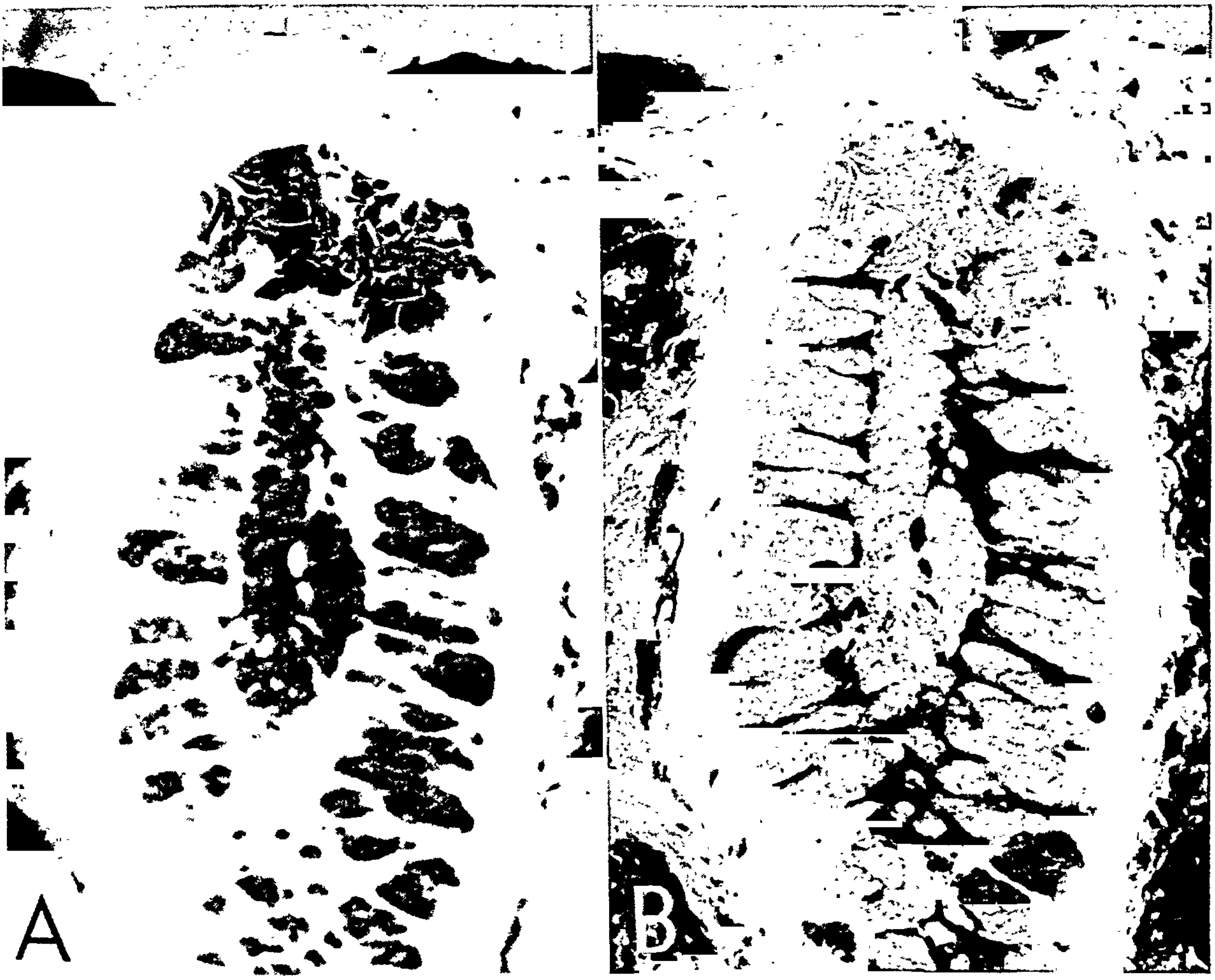

Fig. 4.—Rectal biopsy specimen taken after barium enema, showing barium sulfate crystals within intestinal gland and destructive changes of epithelial cells in contact with crystals, *A*, in polarized light, *B*, in ordinary light (× 540).

Two cases of appendiceal granulomas caused by barium sulfate crystals introduced during barium enema examinations have been reported,[4] and it is possible that the barium gained entry into the appendiceal wall through the lumens of the intestinal glands.

Summary

Histological evidence shows that barium sulfate enters the lumens of intestinal glands during barium enema examinations. It is believed that occasionally this phenomenon can be demonstrated roentgenographically. Destructive changes of the epithelium of the intestinal glands from deposits of barium sulfate crystals may be shown by biopsy specimens taken immediately after barium enema examinations. This may explain the portal of entry and mechanism of formation of barium granulomas of the rectum occurring after barium enemas.

Dr. Joseph Ehrlich, Director of Pathology, interpreted the pathological material.

1475 Grand Concourse (52).

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J.A.M.A., May 28, 1960

LEUKOCYTIC INFILTRATION OF THE UMBILICAL CORD

MANIFESTATION OF FETAL HYPOXIA DUE TO REDUCTION OF BLOOD FLOW IN THE CORD

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and
John A. O'Sullivan, M.D., Cleveland

Leukocytic infiltration was found in 10% of the umbilical cords examined in a preliminary study. The present examination of the cords obtained from 1,000 consecutive deliveries made it possible to correlate the presence or absence of the infiltration with each of a list of maternal and fetal factors. Lymphocytic infiltration of the umbilical cord was most strongly associated with prolonged labor, with a staining of the amniotic fluid by meconium, and with positional abnormalities of the cord. Correlations with inhalation anesthesia, with multiparity, and with fetal tachycardia or bradycardia were suggestive but weaker. Leukocytic infiltration of the cord is therefore interpreted to mean that there has been fetal distress and anoxia due to hindrance of the umbilical circulation.

The significance of leukocytic infiltration of the umbilical cord has been a subject of investigation and speculation for many years. In the early part of this century, such infiltration, as well as round cell infiltrates in other locations, was attributed to syphilis. Controlled studies,[1] however, clearly demonstrated that leukocytic infiltration of the umbilical cord is not due to syphilis. In Beckman's and Zimmer's [1a] report, the microscopic findings in the umbilical cord were correlated with clinical observations on the mothers and their infants. In addition to denying any relationship to syphilis, these authors found that there was no association with either maternal or fetal bacterial infection. They concluded that the cellular infiltrates were the result of mechanical stasis of blood in the course of labor or of delivery and that the presence of such infiltrates was of no clinical consequence to the newborn infant. Recently, Benirschke and Clifford [2] reported a study of placentas and umbilical cords in 1,300 consecutive deliveries. They found leukocytic infiltration of the cord in 10% of cases. They interpreted such infiltration as vasculitis of the cord and implied that such infiltrates may be an indication of intrauterine fetal infection.

Leukocytic infiltration of the umbilical cord was found in about 10% of the cases examined in the first investigation conducted at Saint Luke's Hospital.[1b] One of the impressions obtained from this investigation was that there was apparent association of leukocytic infiltration of the umbilical cord with clinically recognized fetal distress. During subsequent years we have had frequent opportunity to examine microscopically the umbilical cords of infants who died intra partum or in the early postpartum period. The incidence of intrauterine infection was insignificant in the infants on whom autopsies were permitted. On the other hand, death was apparently due to hypoxia in a large proportion of these autopsies. Leukocytic infiltration of the umbilical vessels was found so frequently in these infants that we became convinced of the importance of the observations as an index of intrauterine hypoxia. In 1957 we decided to conduct a controlled investigation to determine whether we could demonstrate a statistically significant association between leukocytic infiltration of the umbilical cord and intrauterine fetal distress.

Method

In this discussion of leukocytic infiltration of the umbilical cord, we refer to infiltration of the blood vessels, primarily the vein. Infiltration of the vein without infiltration of the arteries is common. We have never observed infiltration of the arterial wall without infiltration of the vein. Assuming our interpretation of the progression of the severity of the infiltration to be correct, the earliest manifestation is margination of leukocytes closely apposed to the intima of the vein either in one sector of the lumen or completely around the circumference. In more advanced stages the leukocytes penetrate the wall and infiltrate either in clusters or diffusely. The mural infiltration may be confined to one sector of the wall or more. In intense degrees of infiltration the leukocytes may migrate outside the wall of the vein into the adjacent Wharton's jelly. When one umbilical artery, or both, is infiltrated by leukocytes, the appearance of the infiltrate is similar to that found in the veins. These observations are identical to those previously reported by Beckmann and Zimmer.[1a] We have not observed the cellular infiltration of the surface of the umbilical cord reported by Benirschke and Clifford,[2] nor, in our promptly fixed tissue, have we found bacteria on the surface of the cord, as they described.

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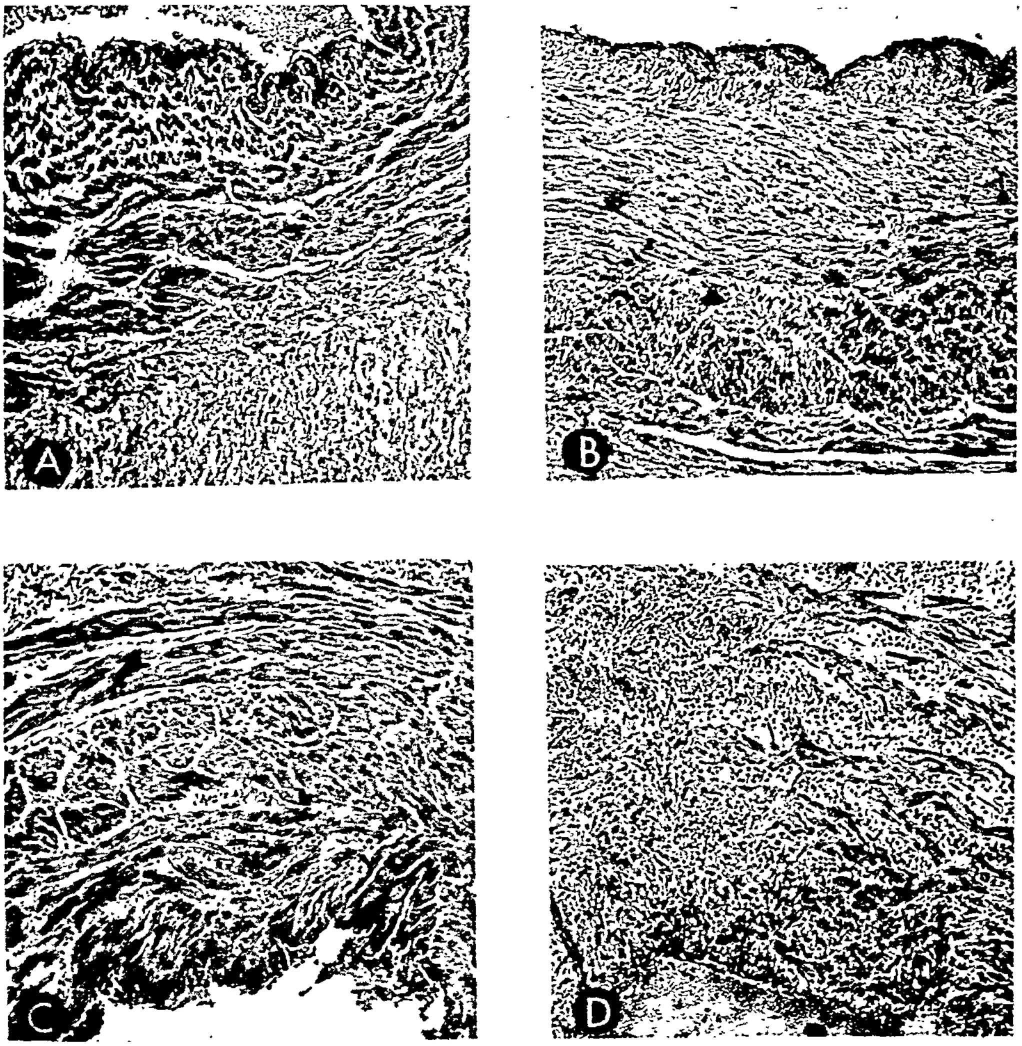
Read before the Scientific Session of the 25th Anniversary Celebration of the Jewish General Hospital, Montreal, Sept. 21, 1959.

We examined umbilical cords in 1,000 consecutive deliveries. The nurses in attendance at the deliveries were instructed to remove two segments of each umbilical cord immediately after delivery of the placenta. One segment, 3 to 5 cm. long, was taken near the placenta and the other, of approximately equal length, near the severed end. The segments were placed immediately in Bouin's fluid, each segment identified in a separate container. A paraffin section of each segment was prepared after fixation and the sections were stained with hematoxylin and eosin. The sections were examined by staff pathologists who had no knowledge of any clinical details related to the specimen. In every case leukocytic infiltration was recorded as being present or absent in one or both of the umbilical cord segments, regardless of the number of vessels affected. After 1,000 specimens had been obtained, one of us (A. J. S.) reviewed all those in which leukocytic infiltration had been observed. The purpose of this review was to obtain a consistent interpretation, by a single observer, of the severity of leukocytic infiltration. The degree of this infiltration was evaluated in the vein and was graded as follows (see figure): ±: margination of leukocytes, with or without sparse subintimal or mural infiltration (94 cases); +: clusters of leukocytes in intramural position, with or without subintimal infiltration (95 cases); ++: intramural leukocytic infiltration, either in large focal clusters or moderately diffuse (41 cases); and +++: marked diffuse leukocytic infiltration, with or without infiltration of Wharton's jelly (15 cases).



Sectors of cross section of umbilical veins, showing variation in appearance from normal vein to intense leukocytic infiltration of vein (medium magnification). *A*, normal vein, no leukocytic infiltration; *B*, slight leukocytic infiltration in interstices of wall; *C*, moderate leukocytic infiltration in interstices and margination of leukocytes on intima; and *D*, intense leukocytic infiltration.

While the tissue study was in progress, one of us (J. A. O'S.) worked independently on the collection of clinical information as recorded on the obstetric record of each patient. The present report deals with 986 single births. All the information collected was transferred to punch cards to facilitate analysis of the data. The clinical data collected and the association of each with leukocytic infiltration of the cord are shown in the table. The significance of the association of pairs of categories was determined from two-by-two contingency tables by the method of Fisher and Yates.[3]

A significant association, with probability less than 0.005 in one tail, was found between leukocytic infiltration of the cord and (*a*) meconium staining of the amniotic fluid, (*b*) positional abnormalities of the cord, and (*c*) prolonged labor. A suggestive association, with probability less than 0.025 in one tail, was found between leukocytic infiltration of the cord and (*a*) general inhalation anesthesia as compared with noninhalation anesthesia, (*b*) grand multiparity, and (*c*) marked slowing or acceleration of the fetal heart rate.

We recognize that the clinical data are sometimes incomplete and sometimes apparently inconsistent. Any such apparent inadequacies are inherent in routinely prepared clinical records. In our opinion, the conclusions we have reached from the present study are more valid than they would be if the clinical recorders had been aware of the information we were seeking. In the present study the significance of degrees of severity of leukocytic infiltration of the cord will not be discussed.

*Data Obtained in 986 Consecutive Single Births to Determine Association of Maternal and Fetal Factors with Leukocytic Infiltration of Umbilical Cord**

Clinical Factors	Leukocytic Infiltration of Cord		
	Yes	No	Total
No. of pregnancies			
First*	53	184	237
2-5*	157	499	656
6 or more	35	58	93
Positive result of serologic test for syphilis (mother)	1	2	3
Rh-negative (mother)	13	71	84
Complications of pregnancy			
Recorded	11	46	57
Not recorded	231	695	929
Duration of labor, hr.			
Less than 18*	211	652	863
18 to 24*	13	44	57
More than 24	17	17	34
Not recorded	4	28	32
Vaginal examination during labor			
Recorded	48	115	163
Not recorded	197	626	823
Meconium staining of amniotic fluid			
Recorded*	26	24	50
Not recorded	219	717	936
Fetal heart rate and rhythm, per min.			
Less than 120*	13	25	38
120-160	199	632	831
More than 160*	10	13	23
Not recorded	22	62	84
Irregular	1	9	10
Rupture of membranes (interval between rupture and delivery), hr.			
Less than 12	88	304	392
Artificial (less than 12)	10	46	56
At delivery	124	331	455
More than 12	21	48	69
Not recorded	2	12	14
Position and presentation			
Vertex	233	717	950
Breech	9	19	28
Transverse	0	1	1
Not recorded	3	4	7
Type of delivery			
Spontaneous	47	120	167
Low-forceps	168	537	705
Mid-forceps	15	26	41
Breech extraction	9	16	25
Cesarean section	6	35	41
Other manipulation	0	3	3
Not recorded	0	4	4
Analgesic agent used			
Meperidine	195	630	825
Alphaprodine	11	14	25
Not recorded	39	97	136
Number of doses of analgesic agent			
1	93	292	385
2	50	174	224
3-5	58	163	221
6 or more	8	20	28
Not recorded	36	92	128
Interval from last dose of analgesic agent to delivery, min.			
Less than 15	1	4	5
15-30	6	50	56
31-45	6	10	16
More than 45	196	587	783
Not recorded	36	90	126
Type of anesthesia			
Spinal*	189	620	809
Pudendal*	2	5	7
Caudal*	3	6	9
General	38	78	116
Not recorded	13	32	45
Duration of anesthesia, min.			
Less than 10	11	61	72
10-20	180	547	727
21-30	28	63	91
More than 30	12	36	48
Not recorded	14	34	48
Fetal distress during labor			
Recorded	13	27	40
Not recorded	232	714	946
Birth weight, Gm.			
Less than 2,500	17	52	69
2,500-3,500	143	451	594
3,501-4,000	63	172	235
4,001-4,500	17	55	72
More than 4,500	4	9	13
Not recorded	1	2	3
Positional abnormalities of umbilical cord			
Cord around neck*	76	162	238
Prolapse of cord*	2	1	3
Not recorded	167	578	745
Resuscitation (oxygen inhalation of the newborn)			
Recorded	26	52	78
Abnormal postnatal course of the newborn			
Recorded	8	20	28
Perinatal deaths			
Stillbirth	2	5	7
Neonatal death	4	11	15
Autopsies	2	4	6

* In calculating association of pairs, data marked with an asterisk were compared with boldface data. Where more than one line of data, in any category, is similarly identified, these data were combined for the calculation.

Comment

Role of Infection.—Infiltrations by leukocytes are commonly attributed to infection. However, it is equally well known that infiltrations by leukocytes can and do occur in the absence of infection. Aseptic tissue necrosis secondary to vascular occlusion is characterized by a zone of leukocytic infiltration on the boundary of the necrotic focus. Stasis of blood in vessels, spontaneous or induced, results in margination of leukocytes when the flow is sufficiently decelerated. If the condition of stasis is prolonged, the leukocytes soon migrate into and around the vessel walls. Such phenomena are common in tissues removed at surgery and are familiar to the surgical pathologist.

Although Benirschke and Clifford[2] implied that leukocytic infiltration of the cord is an indication of intrauterine fetal infection, they freely admitted that the incidence of leukocytic infiltration of the cord is considerably greater than the incidence of clinically evident neonatal infection. They found, as have other investigators, an incidence of 10% of cases with leukocytic infiltration of the cord. It is highly improbable that 10% of infants born in a well-controlled maternity hospital would have acquired an intrauterine infection. We believe, therefore, that no convincing evidence of direct association of leukocytic infiltration of the cord and intrauterine fetal infection has been presented.

Role of Blood Stasis.—Obstetricians have long recognized that fetal distress is clinically manifested by meconium staining of the amniotic fluid, in presentations other than breech, and by gross abnormality of the fetal heart rate or rhythm. It has also been long recognized that the fetus at or near term can survive a more prolonged total lack of oxygen than can the newborn infant.

In a carefully documented study of fetal anoxia, Walker[4] showed a significant association of fetal hypoxia or anoxia with meconium staining of the amniotic fluid and with gross abnormality of the fetal heart rate or rhythm. His conclusions were based on oxygen levels determined in the blood of the human fetus in both abdominal and vaginal deliveries, in the latter half of pregnancy, before and after labor, and in normal and abnormal cases. In all cases the author took a detailed clinical history, and he stated that the length of gestation was accurately known. Inhalation anesthesia was not used in the cases he studied so as to avoid interference with the blood-gas analysis. Although in the report cited Walker emphasized his finding that the oxygen supply and oxygen reserve of the fetus decrease very rapidly, and occasionally, after the 40th week of gestation, may reach fatal levels, he made other important observations. He observed, for example, that oxygen deficiency of the fetus is manifested by passage of meconium when the oxygen saturation of the blood in the umbilical vein is at or below 30%.

If the association of hypoxia and passage of meconium demonstrated by Walker is valid, strength is added to our own observations and conclusions. We have demonstrated a significant association of leukocytic infiltration of the cord with passage of meconium, from which we infer that there is a significant association of hypoxia with leukocytic infiltration of the cord.

We have also demonstrated a significant association of leukocytic infiltration of the cord with stasis-producing positional abnormalities of the cord. We infer, therefore, that the hypoxia and the leukocytic infiltration of the cord are the direct results of reduction of blood flow in the vessels of the cord.

We have shown that leukocytic infiltration of the cord occurs much more frequently than clinically evident meconium staining of the amniotic fluid and more frequently than gross abnormalities of the fetal heart rate. If our interpretation of the significance of leukocytic infiltration of the cord is correct, it would appear that this infiltration is a more sensitive index of intrauterine hypoxia than either the passage of meconium or abnormalities of the fetal heart rate. This assumption leads to the further inference that a severe degree of hypoxia is already present when meconium staining is apparent. The latter inference is supported by Walker's observation of low oxygen saturation of the blood in the umbilical vein when meconium staining is evident. We speculate that it may be possible to detect lesser degrees of fetal hypoxia by colorimetric examination of the amniotic fluid at the time of delivery.

Since the fetus who survives prolonged hypoxia during birth may nevertheless suffer damage to the less resistant higher cerebral centers, and since leukocytic infiltration of the umbilical cord is a more reliable index of fetal hypoxia due to reduction of blood flow, it is suggested that a method is hereby provided for a long-term study of the effect of intrauterine hypoxia on the growth and development of children. The present study is being continued to include an additional 1,000 consecutive deliveries in order that we may evaluate other observations which have not been discussed.

Summary and Conclusions

This is a report of a correlated clinical and pathological investigation into the significance of leukocytic infiltration of the umbilical cord in 1,000 consecutive deliveries at Saint Luke's Hospital. Leukocytic infiltration of the umbilical vein (with or without infiltration of the umbilical arteries) was found in 245 of 986 single births (24.8%). A significant association occurred between leukocytic infiltration of the cord and (*a*) prolonged labor, (*b*) meconium staining of the amniotic fluid, and (*c*) positional abnormalities of the cord. A suggestive association occurred between leukocytic infiltration of the cord and (*a*) general inhalation anesthesia as compared with noninhalation anesthesia, (*b*) grand multiparity, and (*c*) marked slowing or acceleration of the fetal heart rate.

Our observations led us to conclude that leukocytic infiltration of the umbilical cord is due to interference with the normal flow of blood in the umbilical vessels and that it is a more sensitive indicator of fetal distress due to hypoxia than are abnormalities of the fetal heart rate and rhythm or clinical recognition of meconium staining of the amniotic fluid. It is suggested that the examination of the umbilical cord for leukocytic infiltration affords a means for a long-term study of children to determine the effect of intrauterine hypoxia on their ultimate growth and development.

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J.A.M.A., May 28, 1960

PROPHYLAXIS AGAINST STREPTOCOCCIC INFECTION IN AN ADULT RHEUMATIC POPULATION

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and
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Evidence that patients with rheumatic heart disease were not receiving adequate prophylaxis led to an investigation of the reason for this neglect. A series of 101 patients with rheumatic heart disease or past rheumatic fever were studied, first with regard to the severity of their condition and second with regard to the measures they were taking to prevent recurrences. No evidence was found to indicate that either the patient's age or the severity of his heart disease influenced his observance of a program of prophylaxis. The most definite factor increasing the likelihood of such observance was his exposure to the influences of a teaching hospital. In a few instances private physicians seemed to be unaware that a free supply of penicillin was available. Both physicians and patients need to be educated about the need for prophylaxis and the means available.

At the Work Classification Clinic of the Cleveland Area Heart Society, we have been surprised that prophylaxis against streptococcic infection has been prescribed so infrequently for patients referred to us with rheumatic heart disease or past rheumatic fever. Even more puzzling has been the fact that recommendations to institute such prophylaxis have usually been ignored by the referring physician, especially since there is convincing proof of the value of prophylactic programs for patients with rheumatic disease.[1] To determine whether this reflected local practices, we surveyed the recent medical literature for facts about the application of such prophylaxis in adults with rheumatic disease elsewhere. This information apparently was not available. It has been estimated by two active workers in the field that 15% of the rheumatic population is currently receiving adequate prophylaxis against streptococcic infection.[2] In an attempt to verify this shockingly low figure and to elucidate important factors involved in the prescription of prophylaxis for patients with rheumatic disease we have reviewed our recent experiences at the Work Classification Clinic.

Methods and Material

The present study encompasses the last 101 consecutive patients with rheumatic heart disease or past rheumatic fever referred to and evaluated in the Work Classification Clinic of the Cleveland Area Heart Society between June 15, 1956, and May 1, 1959. All except three had unequivocal clinical evidence of rheumatic heart disease as manifested by significant murmurs. Twelve had "pure" aortic disease, 32 had "pure" mitral disease, and 54 had both mitral and aortic valvular involvement. The remaining three patients had presumptive evidence of rheumatic disease: two had typical histories of sore throat followed by polyarthritis and the third had had chorea as a child. Patients with other associated cardiovascular diseases were excluded.

Their clinic records were reviewed with respect to age, sex, severity of heart disease as judged by therapeutic and functional classification of the New York Heart Association,[3] length of time elapsed since the initial episode of activity, recurrences of rheumatic activity, type of prophylactic program, source of clinic referral, and presence of small children in the home. No effort was made to evaluate the strictness of adherence to the prophylactic program. Prophylaxis was considered adequate if one of these accepted programs[4] was being followed: (1) benzathine penicillin G (Bicillin), 1,200,000 units given intramuscularly every four weeks; (2) penicillin, 200,000 units given orally once or twice daily; or (3) sulfadiazine or a related sulfonamide, 0.5 Gm. given twice daily.

Results

The study group of 101 patients included 26 women and 75 men. The ages ranged from 18 to 63 years. Thirty-one patients (30.7%) had no history of overt clinical rheumatic activity at any time. The incidence of a history of acute rheumatic activity was comparable in the various functional classifications (table 1). However, there was a definite relationship between the severity of heart disease and the rate of recurrence of rheumatic activity (table 2). Thus the rate of recurrence increased from 14.7% to 34% to 52.9% as the functional classification increased from I or better to II

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to III or worse. This correlation implies that recurrences of rheumatic activity were associated with deterioration of cardiac function.

At the time of their initial visit to the Work Classification Clinic, 28 subjects (27.7%) were on a prophylactic program prescribed by their physician. Nineteen were receiving therapy with injectable benzathine penicillin G, seven oral therapy with penicillin, and two therapy with sulfonamides; two patients had experienced a recurrence of rheumatic activity while receiving prophylaxis (one with benzathine penicillin G and one with a sulfonamide). Twenty-three patients had had previous heart surgery, i. e., mitral commissurotomy. Of these 23 patients, 9 (39%) were being given prophylactic medication. Five patients had experienced an episode of subacute bacterial endocarditis.

TABLE 1.—*Relation of History of Acute Rheumatic Activity to Functional Classification of 101 Adults with Rheumatic Disease*

Functional Classification	Total Patients, No.	History of Acute Rheumatic Activity No.	%
Class I or better*	34	21	61.8
Class II	50	37	74.0
Class III or worse	17	12	70.6
Total	101	70	69.3

* Includes three patients with no heart disease.

Neither age nor the clinical severity of rheumatic heart disease had a significant effect on the prevalence of the prescription of a prophylactic program (table 3). Exposure to the childhood reservoir of streptococcic carriers was also not a factor in influencing the physician to institute prophylaxis, since there was an equal incidence of prophylaxis in the patients with and those without children of school age or younger in the home, in the 95 cases in which this information was available (table 3).

The incidence of rheumatic prophylactic therapy varied with the source of referral (table 3), being higher in patients treated in a teaching hospital (43.9%) than in those treated elsewhere (16.7%). Any patient who had been hospitalized in a teaching hospital or who was treated as an outpatient at a teaching hospital was considered as having been treated in a teaching hospital, regardless of who was the actual referring physician. Thus, it can be seen that exposure to a teaching hospital increased strikingly the likelihood, but did not assure, that a patient with rheumatic heart disease would receive prophylaxis.

TABLE 2.—*Relation of Recurrence of Rheumatic Activity to Functional Classification of 101 Adults with Rheumatic Disease*

Functional Classification	Patients, No.	History of Recurrence of Rheumatic Activity No.	%
Class I or better*	34	5	14.7
Class II	50	17	34.0
Class III or worse	17	9	52.9
Total	101	31	30.7

* Includes three patients with no heart disease.

TABLE 3.—*Relation of Functional Classification, Age, Presence of Children in Home, and Source of Referral to Prescription of Prophylaxis for 101 Adults with Rheumatic Disease*

Classification	Patients, No.	Prophylaxis No.	%
No heart disease	3	1	26.5
Class I	31	8	
Class II	50	15	28.3
Class III or worse	17	4	
Total	101	28	27.7
Age, yr.			
18-24	18	5	27.8
25-40	45	14	31.1
Over 40	38	9	23.7
Total	101	28	27.7
School-age children or infants in home			
Yes	48	15	31.3
No	47	13	27.7
Total	95	28	29.5
Source of referral			
Treated in a teaching hospital			
Industrial physician	6	3	
Cardiologist	4	1	
Internist	6	3	
General practitioner	5	1	
Staff	20	10	
Total	41	18	43.9
Treated elsewhere			
Industrial physician	7	0	
Cardiologist	5	0	
Internist	9	2	
General practitioner	39	8	
Total	60	10	16.7

Comment

The effectiveness of adequate prophylaxis against streptococcic infection in patients with a history of rheumatic fever in preventing recurrence is well established.[4A] The likelihood of recurrence of rheumatic activity for at least 20 years after the initial attack of rheumatic fever has been shown by Bland and Jones[5] to be substantial and predictable (table 4). Another study has shown a one-in-three chance of developing a recurrence over a 10-year period in a group of patients between 17 and 25 years of age.[6] The most important factor controlling the initial rate and the rate of recurrence probably is the intimate contact with carriers of the group A streptococcus. Once a streptococcic infection develops, the rates are uninfluenced by age.[7] In patients who have suffered a recent attack of rheumatic fever the rate of recurrence has been reported in one study as being 50%.[8] The importance of these facts

TABLE 4.—*Expected Rate of Recurrence After Initial Episode of Rheumatic Fever**

Years After Initial Attack	Recurrence, %
1-5	76
6-10	57
11-15	30
16-20	7

* After Bland and Jones.[5]

is recognized by the American Heart Association, which recommends the following program for prophylaxis.[9]

Prophylaxis for Patients with Rheumatic Disease.—On general principles, a prophylactic program is indicated (*a*) for ambulant or hospitalized patients with rheumatic heart disease and (*b*) for all children and young adults with a well-documented or probable history of rheumatic fever. Penicillin is the drug of choice; sulfadiazine is useful only in patients with penicillin allergy. Recommended prophylactic regimens include the intramuscular injection of benzathine penicillin G, 1,200,000 units every four weeks; the oral administration of penicillin, buffered penicillin G or penicillin V, 200,000 units twice daily; or administration of sulfadiazine, 0.5 Gm. twice daily (0.25 Gm. twice daily for children weighing less than 60 lb. [27.2 kg.]).

A final answer to the question of the length of time prophylaxis should be continued in patients with rheumatic disease is not yet available. This is partly because information about the incidence of clinical streptococcic infections or about carrier states among adults over 40 years of age or among such adults with a history of rheumatic fever is not available. However, as pointed out recently by Miller,[4] the use of penicillin or sulfonamides up to the age of 40 years would cover the 20-year period of high recurrence rate, since most initial attacks occur between the ages of 5 and 20 years. Coverage during this period would also protect the patient during the time he has maximum exposure to the childhood streptococcic reservoir.

We have presented our experience with an adult, nonindigent, employed rheumatic population in an urban community. This population does not differ significantly, as far as age, sex, source of referral, working status, motivation, and functional classification are concerned, from the patients with other forms of heart disease seen in the Work Classification Clinic of the Cleveland Area Heart Society.[10] The age, varying severity of cardiac involvement, types of valvular lesions, incidence of cardiac surgery, and frequency of subacute bacterial endocarditis are fairly representative of an adult working rheumatic population.

Our study group, which resides in an urban community, is not receiving adequate prophylaxis despite the fact that free penicillin and sulfonamides are made available by public funds. The reasons for this failure to apply a sound public health measure are obscure in view of the local interest in heart disease, vigorous annual health campaigns, and generous public support of research, including that by investigators known nationally for their pioneering work in rheumatic heart disease. Is this due to apathy, ignorance, or rejection by the practicing physician or by the patient himself of the value of prophylaxis; or are there economic or other factors?

In a few instances lack of awareness by the private physician of the free supply of penicillin and his charge for an injection may have been responsible. The high employment rate of our population, however, excludes the likelihood that economic factors were of primary significance. Age of patient, severity of heart disease, and the presence of children certainly did not impress the private physician sufficiently to alter the incidence of prophylaxis in this population. The greater acceptance by the pediatrician of prophylaxis for the childhood rheumatic population[11] suggests that practicing physicians attending adult rheumatic patients have not been reached by the educational programs of private and public health agencies. Inadequate dissemination of basic information is suggested by the low incidence of prophylaxis of rheumatic patients exposed to local teaching centers and to such special and sophisticated treatment as cardiac surgery. The present application of prophylaxis in rheumatic adults falls far short of the goals and hopes of devoted investigators and public health agencies to eradicate rheumatic fever.

Summary

The present study reveals a low incidence (27.7%) of measures taken to prevent recurrence of rheumatic activity in 101 adults with rheumatic disease, of whom 98 had unequivocal cardiac involvement. There was a definite relationship between the clinical severity of heart disease and the recurrence of rheumatic activity, implying that rheumatic activity is associated with deterioration of cardiac function. The incidence of prescription of a prophylactic regimen varied with the source of referral and was higher in patients who had been treated in a teaching medical center. There is an obvious need for further lay and medical education to enable adults with rheumatic disease to obtain the unquestioned benefits of prophylaxis.

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EFFECT OF CHLOROTHIAZIDE ON INSULIN REQUIREMENTS OF PREGNANT DIABETIC WOMEN

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At the Joslin Clinic diuretic agents are an integral part of the regimen used in the treatment of pregnant diabetics to prevent the formation of polyhydramnios. Chlorothiazide (6-chloro-7-sulfamyl-1,2,4-benzothiadiazine-1, 1-dioxide) markedly alters the renal excretion of sodium, chloride, and potassium and is a potent diuretic. The question was raised as to whether chlorothiazide, being a sulfonamide, affected insulin requirement. The present study was undertaken to determine any such effect in pregnant diabetic women.

Materials and Methods of Study

The use of chlorothiazide in this diabetic population was begun early in 1958. It has subsequently been used in the treatment of 61 female diabetics throughout the course of their pregnancy. Many other patients were given chlorothiazide at some time during their pregnancy, but these women were eliminated from this study.

The average patient was seen initially in the ninth week and then weekly throughout the course of pregnancy. Chlorothiazide therapy was begun at the first visit. The patients were selected at random. Our cases varied in severity, with several diabetics requiring no insulin and some diabetics having nephropathy. The patients were seen by both medical and obstetric staff members. The women were placed on a diet of 30 calories per kilogram of ideal body weight. It consisted of 200 to 250 Gm. of carbohydrates and 1.5 to 2.0 Gm. of protein per kilogram of body weight; fat constituted the remainder. The diet contained 2 Gm. of sodium chloride daily. The patients were weighed weekly, and the insulin dosage was adjusted as necessary. The average date of confinement was the 36th week. At the time of confinement electrolyte determinations were performed for 43 of the 61 patients. The objective of total management in respect to gain in weight was 12 lb. (5.4 kg.). The patients were seen in the follow-up clinic four to six weeks after delivery.

For the purposes of comparison, a control group of an equal number of patients was selected at random from the pregnant diabetic population of the year 1955. At that time ammonium chloride and acetazolamide (Diamox) were used as diuretics. Their use was begun at the first visit. In addition, meralluride (Mercuhydrin) sodium was given weekly, beginning in the 28th week.

Twenty-eight patients received chlorothiazide, 500 mg. daily, throughout pregnancy. Twenty-five additional patients were given 500 mg. daily until the 28th week and then 1,000 mg. per day until delivery. The eight remaining patients received varying doses of chlorothiazide ranging up to 2,000 mg. per day throughout pregnancy. Potassium supplements were not given.

Results.—In the control group, the 61 patients gained a total of 883 lb. (400.8 kg.), or 14.4 lb. (6.6 kg.) per woman. The insulin dosage from the first until the last clinic visit increased from a total

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of 3,036 units to 5,023 units. This represented a 65% increase in insulin requirements during pregnancy.

The 61 patients given chlorothiazide gained a total of 792 lb. (359.5 kg.), or 13.0 lb. (5.9 kg.) per woman. The insulin dosage increased from 2,523 units at the initial visit to 4,169 units at the last visit. This represented a 65% increase in insulin requirements. Fifty-four potassium levels were determined in 43 of the patients treated with chlorothiazide. The average value was 4.6 mEq. per liter. The normal for the laboratory was 4.0 to 5.0 mEq. per liter. Only two values obtained were below 4.0 mEq.; these were both 3.7 mEq. per liter. The highest value was 5.7 mEq. per liter.

An attempt was made to determine if administration of chlorothiazide had any long-term effect on the insulin dosage. This was done by comparison of the prepartum insulin dose with the postpartum dose. The average postpartum insulin dose for 61 patients was 2 units less per day than the prepartum dose.

Comment

Chlorothiazide increases the renal excretion of sodium, potassium, and chloride.[1] Along with the increase in solute output, the urine flow is also increased.[2] Our 61 patients exhibited a 10% weight reduction with respect to the control group, the weight dropping from 14.4 to 13.0 lb. per patient. Meralluride was used only occasionally in the chlorothiazide treated group to enhance diuresis. In the control group meralluride had to be given weekly, beginning at the 28th week, in order to keep the edema and polyhydramnios to a minimum.

Chlorothiazide seemed to have no effect on the insulin requirements. During pregnancy, the insulin requirement increased 65% in the chlorothiazide-treated group and in the control group. No long-term effect on the insulin dosage was noted. The average postpartum dose of insulin was 2 units less than the prepartum dose. This was not considered to be a significant decrease.

The continued daily use of chlorothiazide may lead to hypokalemic alkalosis. This is usually reversible with the administration of supplements of potassium chloride. In our study the patients were not given potassium supplements. Careful dietary analysis indicated that in the prepregnancy state, the average potassium intake was 3,700 mg. per day. In the pregnancy diets, which were high in protein and in fruits, the average potassium intake was 4,500 mg. per day. This represented an increase of 800 mg. of potassium per day in the diet. It was felt that this increase in potassium intake in the food was sufficient not to warrant the use of potassium chloride supplements. It has been shown that potassium secretion in the urine is dependent on the excretion of sodium.[3] On a 2-Gm. salt diet, less sodium is available for exchange with potassium at the distal tubule. This facilitates conservation of potassium and helps to maintain a normal serum potassium level. The determination of serum potassium level in 43 of the 61 patients revealed that no hypokalemia was present and thus corroborated our impression.

Summary

It is concluded that chlorothiazide, in the doses administered, had no effect on the insulin requirements of female diabetics during pregnancy. Neither did there seem to be any long-term effect of the administration of chlorothiazide on the insulin dosage as there was no significant difference between the prepartum and the postpartum insulin requirements. The serum potassium level was not affected by the use of chlorothiazide in the pregnant diabetic. This was thought to be due to the fact that the diet of a pregnant diabetic is high in potassium.

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The chlorothiazide used in this study was supplied as Diuril by Merck, Sharpe, and Dohme, West Point, Pa.

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THE HEALTH OF THE FEET.—A high proportion of patients seeking treatment from chiropodists can only be given any considerable or lasting relief if they are willing to improve their footwear, and a very large number need no other form of treatment than a change of shoes. . . . Foot health is very largely dependent on adequate function of the toes, especially of the great toe. It follows from this that two things are of paramount importance if trouble is to be avoided: First, the development of this function should not be inhibited—and civilized life from birth onwards can hardly be said to encourage it—though in fact a high proportion of the population never do develop it. Second, once it has been acquired, footwear should not prevent its being maintained and used.—Shoes and Feet, Correspondence, *British Medical Journal,* March 12, 1960.

CLINICAL NOTES

OUTBREAK OF TYPHOID FEVER STARTING WITH A CASE OF PURULENT MENINGITIS

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We are reporting a water-borne outbreak of typhoid fever that was initiated by a case which clinically presented the picture of ordinary, acute purulent meningitis. It occurred in a region that for years had been practically free from typhoid fever.

First Case of Outbreak

History.—On Aug. 28, 1959, a 33-year-old man was admitted to the Wyoming County Community Hospital. He had been well until four days prior to admission, when he became ill, with slight pain in the back and some diarrhea. The back pain improved on application of a heating pad. The diarrhea subsided within 24 hours, and he worked during the next three days. On the day of admission he did not feel well but drove to work; however, he returned home soon, collapsed at 10 a. m., and had a shaking chill followed by profuse sweating. The patient was weak and could not walk. One and one-half hours later difficulty in speaking developed, and three hours later the family physician noticed nuchal rigidity and marked tremor of the extremities. The patient's medical and family history were noncontributory.

Physical Examination.—Physical examination on admission to the hospital showed a well-developed, well-nourished, acutely ill man with a temperature of 103 F (39.4 C). His speech was slurred. The pupils were equal but did not react to light. Ears, nose, and throat showed no abnormalities. Marked nuchal rigidity of the neck, marked Kernig's and Brudzinski's signs, as well as a poker spine were present. The chest was normal. The heart was not enlarged; its rate was rapid, the rhythm regular, and no murmurs were audible. The blood pressure was 134/100 mm. Hg. The abdomen was soft; peristalsis was normal. There was no tenderness or muscle guarding. Liver, spleen, and kidneys were not enlarged on palpation. Marked tremor of all extremities and increased, but equal, reflexes on both sides were observed.

Laboratory Data.—Results of laboratory tests were as follows: urine, specific gravity 1,032, slight trace of sugar and acetone; red blood cell count 5,500,000 per cubic millimeter, hemoglobin level 17.1 Gm.%, hematocrit reading 50%, white blood cell count 16,500 per cubic millimeter, with 86% segmented leucocytes, 2% stab cells, 8% lymphocytes, and 4% monocytes; blood glucose concentration 162 mg.%; nonprotein nitrogen level 36 mg.%. On admission a lumbar puncture was performed, and three blood cultures were taken at hourly intervals. The spinal fluid was cloudy, with a pressure of 200 mm. H_2O. It contained several thousand white blood cells per cubic millimeter, predominantly polymorphonuclear leukocytes. Its sugar content was 23 mg.% and total protein content 124 mg.%. On stained smear, many polymorphonuclear cells were seen but no micro-organisms, in spite of thorough search.

Preliminary Diagnosis.—The preliminary diagnosis was acute purulent meningitis, etiology unknown.

Clinical Course.—The patient was placed on therapy with chloramphenicol, 500 mg. intramuscularly every four hours, and penicillin, 2,000,000 units intramuscularly, every four hours. On the next day his temperature had dropped to 98.9 F (37.1 C), and he was more alert and could speak without difficulty. The neurological signs remained unchanged, however. On the third hospital day, he was markedly confused and his temperature again was elevated to 101 F (38.3 C).

Bacteriological Diagnosis.—The bacteriological picture was as follows. A gram-negative bacillus had been recovered from a pure culture of the spinal fluid and from all three blood samples. It appeared in the form of small coccoid rods, which had grown in plain nutrient broth, on blood plates, and as colorless cultures on Endo plates. This ruled out Hemophilus influenzae, in spite of the morphologic similarity, and suggested that it might be a strain of Salmonella. Thus the cultures were transferred to triple sugar tubes, and, when suspicion of Salmonella typhi arose on the next day, routine differentiating sugar rows were set up. This permitted the bacteriological identification of the cultures as Sal. typhi on the next day. They were also readily agglutinated by specific antityphoid serum in high dilutions. Later on, the isolated strain was bacteriophage-typed in the New York State Department of Health, division of laboratories and research, in Albany, N. Y. It belonged to group

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From the Internal Department, Wyoming County Community Hospital (Dr. Wagenhals) and the County Laboratories of Wyoming and Genesee (Dr. Tannenberg).

type E1, according to Craigie's classification. The bacteriological identification work was simultaneously and independently performed in two of our laboratories, the Wyoming County Laboratory, Warsaw, N. Y., and in the Genesee Laboratory, Batavia, N. Y., respectively.

In the third week the patient developed a positive reaction to the Gruber-Widal test, with a titer of 1:2,560 against O-antigen and of 1:640 against H-antigen.

Further Clinical Course.—The patient's clinical course developed as follows: On the fourth hospital day he became extremely excited, so that constant attendance was required. His status somewhat resembled delirium tremens. Some of his friends stated that alcoholism had been a problem for him in the past, although his wife denied recent abuse of alcohol. The extreme excitability and confusion lasted for about 48 hours but cleared with the return of the body temperature to normal on the seventh hospital day.

After definite identification of the organism on the fourth hospital day, penicillin therapy was discontinued and chloramphenicol was given orally in a dosage of 500 mg. This dosage was continued to the fourteenth hospital day, when it was reduced to 250 mg. every four hours. The patient's condition rapidly improved after the return of his temperature to normal, and he was kept in the hospital for 10 more days after clinical recovery, for a total of 17 days. Three stool specimens and one urine specimen were negative for Sal. typhi prior to discharge. Chloramphenicol therapy was continued for a total of four weeks, and the patient has remained asymptomatic according to the report of his family physician.

Epidemiologic Follow-up

On our identification of Sal. typhi as the incitant of the purulent meningitis, the Wyoming County Health Department and the State Health District Officer for Livingston County discovered the source of the infection. The patient's aunt was a known typhoid carrier, according to the files in the State District Health Office. This woman had spent two weeks in a rented summer cottage by a lake and had had several family reunions during that time. Our first patient, the man discussed above, had visited this cottage about 15 days prior to his admission. Soon afterwards a second relative of the carrier was admitted to our hospital and ordinary typhoid fever, without complications, was diagnosed. She had been a guest at the cottage 17 days prior to admission. Two more persons developed typhoid fever from the same source. They were treated and their disease was diagnosed in a hospital in Rochester, N. Y., and in the state of Illinois, respectively. These patients were children of families who occupied the cottage for two weeks after the carrier had left. One child developed the disease after an incubation period of about 25 days, the second after 39 days. In all four cases the disease had been incited by a bacteriophage type El strain of Sal. typhi, the same as the carrier's.

Source of Infection.—The source of infection was established by collecting water samples from the well that served as drinking water in the respective cottage which, on routine examination, contained coliform bacilli in large quantities. To attempt isolation of Sal. typhi from the small amount of water usually used for the routine test for coliform bacilli appeared futile. We intended to filter a larger amount of the suspicious water through a bacteria-tight filter and to incubate the filter membrane in an enrichment broth for typhoid bacilli. A Seitz filter membrane or Millipore filters, or any other self-fabricated, so-called ultrafilter seemed to fit our purpose. On our request the Wyoming County Health Department submitted a gallon bottle of the drinking water from the particular cottage about four weeks after the typhoid carrier had vacated the cottage. A few days prior to collection, the sanitary engineer of the Wyoming County Health Department had added some fluorescein to the toilet of the cottage in question. The drinking water sample then submitted showed evidence of fluorescein, proving access of sewage material from the toilet to the drinking water supply by virtue of inefficiency of the old septic tank. Of this water, two portions of 250 and 750 ml., respectively, were run through a bacteria-tight filter. The filters were then incubated in tetrathionate enrichment broth for 24 hours, and Sal. typhi, which again was identified by the division of laboratories and research as belonging to the bacteriophage type El, was recovered from both portions.

Comment

The facts reported are remarkable for the following reasons. 1. The first case of a small outbreak of typhoid fever appeared clinically as one of ordinary purulent meningitis. 2. The disease was spread by a typhoid carrier's use, for two weeks, of the toilet facilities of a rented cottage that had an old septic tank. She thereby infected the well water supply of this cabin so thoroughly that 2 of 16 persons, who visited the cottage for one day, contracted the disease. Two additional persons of twenty-five who lived in the same cottage, or visited there, for two weeks after the carrier had left, contracted the disease. 3. The typhoid bacilli survived for at least four weeks in the ground water after the carrier had left the cottage, and it was possible to recover them in water portions of 250 and 750 ml. by bacteria-tight filtration and by culturing the filter membranes in tetrathionate enrichment broth.

The reported case of typhoid meningitis differed clinically from an ordinary purulent meningitis, inasmuch as the patient's condition failed to show the customary general improvement on the day after administration of adequate doses of antibiotics, although the body temperature had readily dropped. The extreme confusion and excitability that developed on the fourth hospital day and lasted for 48 hours were also unusual. Stuart and Pullen,[1] in a report on 360 cases of typhoid fever observed between 1939 and 1944 in New Orleans, saw psychotic symptoms in 1.94% of their patients after all other clinical evidence of disease had disappeared. The purulent spinal fluid and the high white blood cell count of 16,500 per cubic millimeter, with a differential count of 86% polymorphonuclear leucocytes on the first day of admission of our patient, at first did not suggest typhoid fever, which is usually associated with a leukopenia, either. However, Cole,[2] in 1904, in the first review of purulent typhoid meningitis covering 14 cases, already reported the predominance of polymorphonuclear leucocytes in the spinal fluid in most of these cases, and Stuart and Pullen,[1] in 1946, mentioned a transient rise in the number of leucocytes in the first few days of the disease, followed by a fairly rapid and progressive leukopenia.

The long duration of the incubation period of from 15 to 39 days in our small series undoubtedly depended on the small number of bacilli that brought the infection about.

Involvement of the central nervous system in the form of meningism is no rarity in the course of typhoid fever. Stuart and Pullen,[1] for instance, observed 46 cases with central nervous involvement, but in only 1 were typhoid bacilli recovered from the spinal fluid by smear or culture. "Typhoid" is derived from the Greek word τυφος, meaning fog or fogginess of the senses, and the disease was known as "Nervenfieber" (nerve fever) in the German literature up to the middle of the last century.

Our recovery of Sal. typhi from pumped well water, about four weeks after the typhoid carrier had left, is of interest. We consider the method described the simplest and most efficient to examine larger quantities of water for such organisms. The survival of the typhoid bacilli in the soil and well water for four weeks is perhaps surprising, but the literature on bacteriology cites a number of instances in which typhoid infection occurred from drinking the water of streams which had been polluted by wells that were far upstream. Our case occurred in the month of September in comparatively mild weather. The ability of Sal. typhi to survive for some time in water that contains sewage material is not too miraculous, if the studies by Braun and Cahn-Bronner[3] (1921-1922), on the minimal requirements of Sal. typhi are recalled. They established that mediums containing only mineral salts, together with ammonia as a source of nitrogen and various organic acids as a source for carbon, were sufficient to support the growth of Sal. typhi. Similar observations were made by Fildes and co-workers in 1933.

Review of Literature

In the literature we found no record of another outbreak of typhoid fever that was initiated by a case of purulent meningitis. In our opinion, the first case of purulent typhoid meningitis reported is that of Neumann and Schaeffer[4] in 1887, only seven years after the first isolation of the typhoid bacillus. These authors were not entirely sure whether or not they were dealing with a typhoid meningitis in spite of their isolation of typhoid bacilli from the meninges, because their patient did not show the usual manifestations of typhoid fever in the intestine. Thus, Cole,[2] in the first review of purulent typhoid meningitis, omitted this case and recorded as the first case one observed in 1893 in Bohemia. In 1912, however, Lemierre and Joltrain[5] eliminated this reason for doubt. They collected six cases in which purulent typhoid meningitis apparently constituted the primary localization of the disease, without preceding intestinal manifestations. Baumgartner and Olsen,[6] in their review in 1920 of purulent typhoid meningitis, reported 2 more such cases among the 23 collected since Cole's report.[2] Up to that time, all 37 cases of purulent typhoid meningitis reported had been fatal. Among these patients only one was an infant under 1 year of age (4 months), nine were children between 5 and 10 years of age, and only one was older than 50 years. The onset of meningeal symptoms was observed in most of the cases on the 10th day or later and in only four cases between the 1st and 4th day of the disease. Hageman, in 1938, added from the literature 23 additional fatal cases of purulent typhoid meningitis and observed the first case with recovery in a 42-year-old man who was admitted to the hospital on the 26th day of his disease and showed typhoid bacilli in the spinal fluid and stool, but not in the blood.

Reviews of Salmonella meningitis specifically excluded cases of typhoid meningitis up to the work of Henderson[7] who, in 1948, collected 147 cases, beginning with the first case of Sal. paratyphi-B meningitis reported by Ghon in 1907. Later reviewers, namely Beene and co-workers[8] (1951) and Smith and co-workers[9] (1954) reported typhoid meningitis together with Salmonella cases, because the typhoid bacillus was by then considered a member of the Salmonella group. Clinical differences between meningitis caused by Sal. typhi and other members of this group are, however, still great. Typhoid meningitis in infants is rare, while that due to other Salmonellae is at least four times as frequent in infants as in adults. Both are rare diseases but frequent enough to deserve consideration. Bahrenburg and Ecker, in the first comprehensive review of Salmonella meningitis in 1937, covered 34 cases; Ramon Guerra, in 1940, collected 59 cases; Neter reviewed cases up to 1944; Henderson,[7] in 1948, chronologically listed 147 cases, including 6 of his own observation. During the next three years, Beene and co-workers[8] collected 81 new references, with a total of 235 patients. Their reference table includes 18 papers that dealt with typhoid meningitis. Smith,[9] in 1954, collected 16 new cases of Salmonella meningitis, among them 2 cases of typhoid meningitis (Ripy 1950, Chigier[10] 1953). Since then, a few new cases of Salmonella meningitis have been reported every year. They were seen in the United States, in Western Europe (England, France, Germany, and Italy), more recently in Poland, Czechoslovakia, Israel, Cuba, Mexico, China, India, Africa, French Polynesia, and Malaya. In most of these cases recovery was observed as the result of administration of adequate doses of antibiotics. In 1950 Saphra reported from the New York Salmonella Center 174 fatalities, on the basis of a review of 3,279 cultures, with the exclusion of Sal. typhi; 34, or 5.8%, of the victims were infants, most of whom died of meningitis.

Since 1950, we have found in the literature reports of five cases of typhoid meningitis in adults (Gordon-Smith and Marsten,[11] 1951, one case in England; Ramirez-Boettner,[12] 1951, one case in the southern United States; Gadrat and co-workers,[13] 1954, one case in France; Bhattacharjee, 1954, one case in India; and Kibel and McNair,[14] 1958, one case in Central Africa). Of these, only the case of Bhattacharjee is not acceptable, since it lacks bacteriological and serologic proof. During the same period, purulent typhoid meningitis was reported in nine infants: Hoering and Petersen,[15] 1950, one fatal case each; Ripy,[16] a 13-month-old infant, who recovered, in the United States, 1950; Chigier,[10] a 3-month-old infant, who recovered, in Israel; Despirito and Santagata,[17] 1954, one case in the United States; Powell,[18] 1956, an infant aged 21 days, perhaps the youngest recovered patient whose case was recorded, in Texas; Khiari and Renoux,[19] 1956, one case, in Tunis; and Shah and Gandhi,[20] 1958, two cases, in India.

Summary

A case which, on the patient's admission to the hospital, clinically appeared to be an ordinary acute purulent meningitis, proved to be a case of typhoid meningitis in an adult. This case ushered in a small outbreak of typhoid fever in an area that for years had been practically free from typhoid fever. The patient was successfully treated with chloramphenicol.

The infection was water-borne and originated from a carrier who lived for two weeks in a summer cottage near a lake. Two persons were infected during her stay at a family reunion at the cottage. Two more persons were infected when they occupied the same cottage for two weeks immediately after it had been vacated by the carrier.

Four weeks after it had been vacated by the carrier, typhoid bacilli were recovered from the well water that supplied the cottage by filtering portions of 250 and 750 ml. through a bacteria-tight Millipore filter and incubating the filter membranes in enrichment broth. The bacterial strain recovered from the carrier and all sick persons, as well as from the well water of the cottage, belonged to bacteriophage-type E1.

This is the first case in which an outbreak of typhoid fever was initiated by an apparently ordinary purulent typhoid meningitis. The speedy bacteriological recognition of the incitant made recovery of the patient possible and terminated the outbreak of a possibly widespread epidemic. The review of the literature further indicates that, during a period in which typhoid fever was not uncommon, purulent typhoid meningitis was rare but occurred usually in adults; up to 1920, only 1 among 38 cases was observed in an infant below 1 year of age, while during the last decade the number reported in infants has doubled that in adults. The first case of typhoid meningitis was reported in 1887, the first caused by other Salmonellae (paratyphi B) in 1907. The incidence of Salmonella meningitis is, however, rapidly increasing, nearly 250 cases having been reported between 1907 and 1950 which were observed in the United States; Western Europe, particularly Germany, France, England and Italy; and more recently in Poland, Czechoslovakia, North, Central, and South Africa, Mexico and Cuba, French Indonesia, and English Malaya. Most of these cases were observed in infants; the outcome depends foremost on a speedy bacteriological diagnosis and the availability of effective antibiotics.

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PERSONALITY DECOMPENSATION AFTER HYPNOTIC SYMPTOM SUPPRESSION

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With the renewal of interest in hypnosis, an increasing number of physicians are finding it a useful and relatively simple therapeutic tool. However, hypnosis is not entirely innocuous. Unless cases are selected with care and therapy is wise, hypnosis may result in symptoms more serious than those for which the patient was originally treated. This paper presents such a case, in which use of hypnosis to suppress an undesirable symptom resulted in development of acute, severe personality decompensation. Furthermore, the case illustrates how factors in a patient's history can clearly contraindicate this form of hypnotherapy.

Report of a Case

The patient was a 41-year-old married man with a fear of flying. As a successful sales executive with a large industry, he often had to make trips throughout the country; for 15 years he had traveled, by either airplane or train, with no particular difficulty. About two years before the onset of his present illness, he had traveled on a particularly rough flight and after this began to notice a growing aversion to airplanes. This aversion developed, in about a year, into a phobia against air travel. He was intensely afraid of boarding an airplane to take a flight, afraid of the sensation of flying, and afraid he would be killed in an airplane crash.

This fear was no real handicap, since he could fulfill his duties by taking overnight trains. The other executives ridiculed him, however, and "It got to the point where even my secretary depreciated me." Because of this social pressure, and his attendant feelings of embarrassment and inferiority, he resolved to see a hypnotist, to have the fear "hypnotized away."

The hypnotist repeatedly assured him that hypnosis would eradicate his fear and enable him to fly. Hypnotic suggestions were begun without a personal history being taken. The sessions were held for one hour per week for six weeks. At each session, the patient was placed in a "medium" trance and the entire flight, from ticket purchase to landing and debarkation was repeatedly reviewed in the patient's imagination, while the therapist assured him at each step that "Everything was all right."

During the trance, the patient was told, for example, "You are now sitting in the plane and the motors are roaring. You feel calm and relaxed. The plane is moving faster and is climbing up and off the ground. Relax completely . . . you feel calm . . . and relaxed. . . ."

After the sixth session, the patient made arrangements to fly to an executive meeting. The patient later said that the flight was "mildly rough," but that he felt only a few uneasy moments, rather enjoyed the trip, and felt pleased to have flown successfully.

On the day after the flight, he woke feeling morose and despondent, "let down . . . depressed . . . like doom was hanging over me." After the initial episode of depression he lost his appetite and be-

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From the Forest Hospital.

came jittery. He masturbated three times during the afternoon. The jittery feeling gave way to intense feelings of dread and anxiety. He became afraid to eat, sleep, or even leave the hotel. His panic was accompanied by multiple somatic complaints, including tachycardia, abdominal cramps, back pain, and diarrhea. His symptoms remained intense until he called his wife and asked her to come and bring him home. After this, they decreased somewhat, although once at home he became "afraid of everything," including sexual relations with his wife, eating, sleeping, being alone, and the people at work. Meprobamate (Miltown) and dextro amphetamine (Dexedrine) sulfate, prescribed over the telephone by the hypnotist, did not help.

"Things," he noted, "seemed to have a strange symbolic meaning." He found himself analyzing everything he thought, said, and did, searching for hidden reasons and meanings. Once, while watching television, he panicked when seeing a drum majorette marching with a baton. He could not eat, sleep, make decisions, or have sexual relations with his wife. For the most part, he remained in bed, trembling and afraid to move.

History.—The patient's history revealed him to be a person whose entire life, prior to the episode of acute personality decompensation, had been active, aggressive, and sometimes hostile. He lived vigorously and appeared happy and successful. He had been happily married for 15 years; he had been employed by the same company for 17 years and had been given a number of promotions, received excellent remuneration, and handled responsible duties. He was active in his community's civic life and in adult education, having served as both teacher and moderator. He and his wife were active socially, with a circle of good friends. He was a good father for his children. Beneath this superficial appearance of health, however, there was considerable personal turmoil. As early as 1945, he had consulted a psychiatrist because of difficulty in making decisions and concern over compulsive masturbation accompanied by sadistic fantasies. After a limited period of supportive psychotherapy, he felt relieved enough to discontinue treatment, with the consent of the psychiatrist.

Despite a grandiose estimate of his creative ability and intelligence (both in fact outstanding) he was conservative and "practical" in his expectations of life and extremely cautious in managing money. He worried almost continuously about putting aside money for future security and was usually saving money in cookie jars for various projects for himself and his family. Before the airplane trip, even though he felt life to be truly satisfying, he often wondered why he should be so happy, in love with his wife and children, and secure in his job, with a large income. He would often wake up in the morning thrilled at the sight of his children and the beauty of his home.

He was always loud, domineering, and forceful, overbearing toward his wife and children, and fond of asserting his opinions over others in verbal contests. Yet, paradoxically, he jokingly said of himself, "I'm a very religious man—a devout coward." He said he was afraid of pain, fights, or violence of any kind and that he often fainted when injected with hypodermic needles. He disliked being in the house alone and would find reasons to go out. On his job, the patient functioned largely as a "creative" sales manager, using his vivid imagination to originate advertising and sales campaigns. This same vivid imagination served him in other ways. It provided masturbatory fantasies of flagellation, in which he beat women on the vulva with a whip and raped them.

He was a virgin when he married and was never promiscuous during his marriage, but he was proud of the aggressive way he looked at most women and of the way he "mentally undressed them." In spite of the lurid, sadistic thoughts he had while looking at women, however, he laughingly emphasized the fact that he would be "scared to death to actually approach one."

The patient is the second of three children. His brother is three years older than he, his sister three years younger. He describes his father as a kind but violent man and his mother as a loving, sensible woman for whom he professes a deep affection. He recalled that the first time he felt an overwhelming feeling of terror was after stealing his father's fountain pen. He accidentally dropped the pen, lost it down a hot-air register, and became intensely afraid of what his father would do.

It was significant that his early years were filled with a continuous struggle to compete with his brother. He insisted on doing everything that his brother did. When he was 12 years of age, his mother sent him away for eight months to live with his grandmother, in an effort to stop the continuous fighting. At about the age of 16 years his hostility and aggressiveness toward his brother came to an end. He was then consistently able to outdo his brother and "beat him up."

Therapeutic Course.—The goal in treating this patient was to restore his personality to its status before the airplane trip. For this purpose, a suppressive attitude was taken, including agreement that the patient would not attempt to fly again.

During the first weeks in the hospital, the patient was extremely anxious, with most of the vegetative symptoms of anxiety. Sedation and rest were encouraged. The patient was repeatedly reassured that he could regain his premorbid ego state. During this stage of treatment, he talked constantly about his attitudes (sadistic, aggressive, hostile, competitive, and domineering), reemphasizing his self-image as a "complete fiend" and asserting his guilt because of these attitudes.

He decided that he had arrived at a transitional point in his life and that he would have to change, move on, grow, and develop. He felt, moreover, that his "old" personality had got him as far as it could in the business world, that he now needed to become a more passive, accepting administrative personality in order to continue his climb in the hierarchy. He resolved to stop his compulsive masturbating, an easy accomplishment since, at this stage, he was intensely phobic about masturbating.

As he responded to reassurance and the pressure of his phobias lessened, a compulsive facet of his character became more apparent. He became indecisive and unsure of himself. He demanded that the therapist give him guiding principles with which to formulate decisions and would debate endlessly all the possible aspects of the most trivial phenomena, never coming to any conclusions.

After eight weeks the phobias had lessened and his appetite began to return. He developed an obsessional concern about the future, expressed in such questions as, "What if I lose all my money?" "What if I can't meet the home payment?" and "Who will take care of my children when I am dead?"

After about 14 weeks, he complained of his sexual disinterest and the sense of guilt he felt concerning his sadistic masturbatory fantasies. When it was pointed out that guilt and shame were necessary components of his masturbatory fantasies and that they were needed to keep his omnipotent feelings in control, he finally was able to accept the necessity for his compulsive masturbation. In keeping with the goal of therapy, he was encouraged to do just that.

On resumption of the masturbatory and presleep fantasies, his sleep improved and he began to have sexual relations with his wife. He found that he could not discuss these fantasies with the therapist and still have them "work," so they were excluded from the content of his interviews.

Finally, the patient was discouraged from pursuing his "development" further. He was told that his complicated check-balance system could function undisturbed without causing any more trouble. With further reassurance, he was able to leave the dependent relationship with his therapist and resume his usual way of life.

Comment

It has been shown in an experimental situation[1] that hypnotic suppression of symptoms can result in the appearance of substitute symptoms of equivalent psychological value. The newer symptoms were found to occur either at the same level of psychosexual development (arm paralysis substituting for torticollis) or at a more regressive level (vomiting, gagging, and upset stomach substituting for arm paralysis). The new symptom could be shown to have an equivalent value in the subject's value system (e. g., an ugly facial rash substituting for obesity as a means for the subject to "show off" in an unattractive way). The total amount of morbidity was also equivalent. Thus, nothing helpful was accomplished for the patient, except for a redistribution of the stress focus and possible proof that the symptoms were of emotional origin.

In the patient discussed here, hypnotic removal of the airplane phobia resulted in substitution of a generalized mild state of anxiety, in the period before the airplane trip. After the trip, the patient experienced profound decompensation of the entire organization of his personality, developing multiple physical and psychological symptoms. His reaction was similar in some respects to the phenomenon of voodoo death, in which natives of certain tribes die an apparently psychophysiological death as a result of violating a tribal taboo. It seemed as if, in taking the plane ride, he had violated a taboo. In fact, he thought of his subsequent difficulties as punishment for wrongdoing.

Because of the nature of the suppressive psychotherapy used in managing this patient's problem, the meaning of flying and its significance in his life were not worked out. It seems apparent, however, that his fear of flying was more than a simple conditioned reaction to a previously frightening flight. The phobia, in fact, was a warning signal that flying represented a serious danger to him, for unconscious or internal reasons.

In view of the patient's history, which included compulsive masturbation with sadistic fantasies, difficulties in making decisions, fears of being alone, and fears of physical injury, the airplane phobia was obviously related to some more central issue. Knowing this, the hypnotist should have refused hypnotic symptom suppression as a treatment method, advising the patient instead either to live with this relatively minor inconvenience or to seek out an etiologically oriented therapy.

Summary

Hypnosis is effective for symptom removal. Symptom removal can be hazardous, however, and should not be used when the symptom is related to an obsessive-compulsive system or to a serious personality, character, or ego defect. As emphasized many times before, an adequate history and diagnosis are essential to the use of hypnotherapy, as is knowledge of psychodynamics and personality structure.

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NEW ALLERGIC REACTION TO FURALTADONE

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In the past six weeks we have observed two patients who have had an identical and unusual reaction while being treated with furaltadone (Altafur), which is a synthetic nitrofuran derivative. This reaction was manifested subjectively by diplopia and objectively by paresis of the lateral rectus muscle. In both cases the diplopia cleared with cessation of therapy. One patient was treated with antihistamines. The other patient was not treated specifically for the reaction. Clinically, the diplopia cleared earlier than the measured paresis of the lateral rectus muscles.

Report of Cases

Case 1.—A 35-year-old woman developed swelling, redness, and heat in her left index finger in November, 1958. The symptoms lasted for a short time and then disappeared but kept recurring over nine months. A biopsy of the soft tissue was performed in August, 1959, revealing only necrotic fat tissue. Since subsequent roentgenograms showed bone destruction, a biopsy on the bone was performed in October, 1959, from which no diagnosis could be made, however. Cultures of the removed tissue were negative, as were results of all other diagnostic tests carried out in an attempt to determine the etiology of the bone lesion. The finger continued to be swollen, tender, painful, and red. The sections were therefore sent to a nationally known pathologist for his opinion of the lesion. He believed that it represented a low-grade osteomyelitis. Since we did not know the causative organism, we decided to attempt treatment with furaltadone.

The patient was placed on furaltadone therapy, 250 mg. every six hours, on Nov. 20, 1959. On Dec. 10, 1959 and again on Dec. 11, 1959, she had chills and fever, lasting about five hours, although no cause could be found. She was maintained on the medicament, and the symptoms did not recur. On Dec. 21, 1959, the finger seemed to be definitely improved, and the therapy was continued. On Jan. 4, 1960, the finger showed only swelling, with no redness, heat, tenderness, or pain. Consequently the patient was started on ultrasonic treatment in an attempt to loosen up the stiffness. On Jan. 11, 1960, she developed diplopia. At first this was manifested in the evening only. Ophthalmological consultation on Jan. 14, 1960, revealed an esophoria of 6 degrees at 6 meters, and of 3 degrees at ⅓ meter. Diplopia could be elicited with the red lens, and separation was greatest on looking to right and left. A diagnosis of bilateral paresis of the lateral rectus muscles was made. Five days later diplopia was constant throughout the day. Esotropia was 20 degrees at 6 meters and 18 degrees at ⅓ meter. On Jan. 26, 1960, the esotropia measured 36 degrees at 6 meters and 24 degrees at ⅓ meter.

On Jan. 27, 1960, because the diplopia continued, the therapy with furaltadone was stopped. The patient had also been taking methamphetamine (Desoxyn) hydrochloride for weight reduction over several months, but was taking no other medicaments. The methamphetamine intake was discontinued at the same time. By Feb. 4, 1960, the diplopia had improved, and prism measurements showed esotropia of 35 degrees at 6 meters, and of 30 degrees at ⅓ meter. The idea of treating her with ACTH or cortisone was entertained, but, because of the infection in the finger, it was decided to try therapy with antihistamines first. On Feb. 11, 1960, the diplopia became markedly better and occurred only occasionally. On Feb. 19, 1960, the diplopia was entirely gone, although objectively a moderate esophoria of 20 degrees at 6 meters and 16 degrees at ⅓ meter remained. The finger at that time was clinically completely well. The patient resumed methamphetamine therapy for weight reduction and since then has not had recurrence of the diplopia.

Case 2.—A 73-year-old man underwent amputation of his left leg above the knee in June, 1959, because of gangrene of the foot secondary to severe arteriosclerosis obliterans. On June 11, 1959, coagulase-positive Staphylococcus aureus and Pseudomonas were cultured from the infected stump. He was treated with penicillin and chloramphenicol (Chloromycetin), after which the local infection cleared. On Aug. 11, 1959, he developed multiple boils over his entire body. Chloramphenicol therapy was tried again, but to no avail. Consequently, administration of oleandomycin phosphate was begun. Since by Aug. 18, 1959, no improvement was evident, he was started on therapy with streptokinase-streptodornase (Varidase), orally given phenoxymethyl penicillin (Pen-Vee), and dexamethasone (Decadron); multiple abscesses were incised and drained. Again little change occurred in the lesions, so that therapy with erythromycin propionate was begun and continued for one week. The patient remained extremely ill, however, with several hundred boils over his entire skin surface. On Sept. 3, 1959, therapy with furaltadone, 1 Gm. daily in divided doses, was begun. The patient's condition showed marked improvement with this therapy. It was discontinued on Sept. 21, 1959, at which time most of the lesions were cleared up. Lesions recurred, however, so that the patient was again given courses of furaltadone; each consisted of 30 tablets, with 1 tablet taken every six hours on Nov. 25 and Dec. 30, 1959, and on Jan. 9, 1960.

On Jan. 12, 1960, while making a house call, it was brought to the attention of the examining physician for the first time that the patient had had diplopia intermittently for the previous two months. Questioning revealed that this seemed to coincide with the periods during which he had taken the furaltadone. Inasmuch as we had just seen another patient who developed diplopia while taking furaltadone, treatment with the drug was stopped, after which the diplopia disappeared in about 12 days.

Since the patient was bedfast at home, accurate measurements of diplopia could not be made. At about 10 ft. there was an uncrossed separation of about 6 in. With use of the red glass and a light, the diplopia disappeared in primary position at 12 in. but recurred on gaze to the left. Diplopia did not occur on gaze to the right. A diagnosis of left lateral rectus palsy was made. On March 15, 1960, reexamination showed no trace of diplopia with a red lens on extreme left lateral gaze.

Comment

We have observed two patients who developed diplopia while taking furaltadone. In both cases it was determined that the diplopia was due to a paresis of the lateral rectus muscles, one bilateral and one unilateral. In both patients the paresis slowly improved after discontinuance of therapy with the drug. A personal report, dated March 1, 1960, from the medical director of Eaton Laboratories, who manufacture the brand of furaltadone given these patients, states that they have reports of four cases of transient diplopia, which cleared entirely on discontinuance of administration of the drug. They had no other report of ocular manifestations and were at a complete loss to explain the occurrence. Evidently it had not been determined previously that the diplopia was due to a paresis of the lateral rectus muscles. The mechanism of this apparent toxic response to the drug has not been determined.

Summary

Two patients developed diplopia caused by paresis of the lateral rectus muscles while they were on therapy with furaltadone (Altafur).

2615 Eye St. (Dr. Loftus).

COUNCIL ON DRUGS

Report to the Council

The Council has authorized publication of the following report.

H. D. Kautz, M.D., *Secretary.*

CURRENT STATUS OF THE THERAPY OF LEPROSY

James A. Doull, M.D., Washington, D. C.

In the search for a cure for leprosy, scientists are deprived of two of the most powerful tools of the experimental laboratory—a method of cultivation of Mycobacterium leprae and a susceptible animal. If the leprosy bacillus could be cultivated on an artificial medium, the bactericidal action of drugs and antibiotics might be determined rapidly, and, if a true prototype of human leprosy could be produced in animals, the effectiveness of drugs might be studied in an even more convincing manner. In the absence of such a direct approach, the most logical leads are to be found in the action of drugs on those pathogenic mycobacteria that can be cultivated and against mycobacterial diseases that are transmissible to laboratory animals. Advantage has been taken, in particular, of information that has been gained in the "screening" of drugs against Mycobacterium tuberculosis and in the treatment of patients with tuberculosis and experimental tuberculosis. Analogy with tuberculosis has failed in many instances, most notably in the case of isoniazid (Armazide, Cotinazin, Dinacrin, Ditubin, Inh, Isoniazid, Niconyl, Nicozide, Nydrazid, Rimi-

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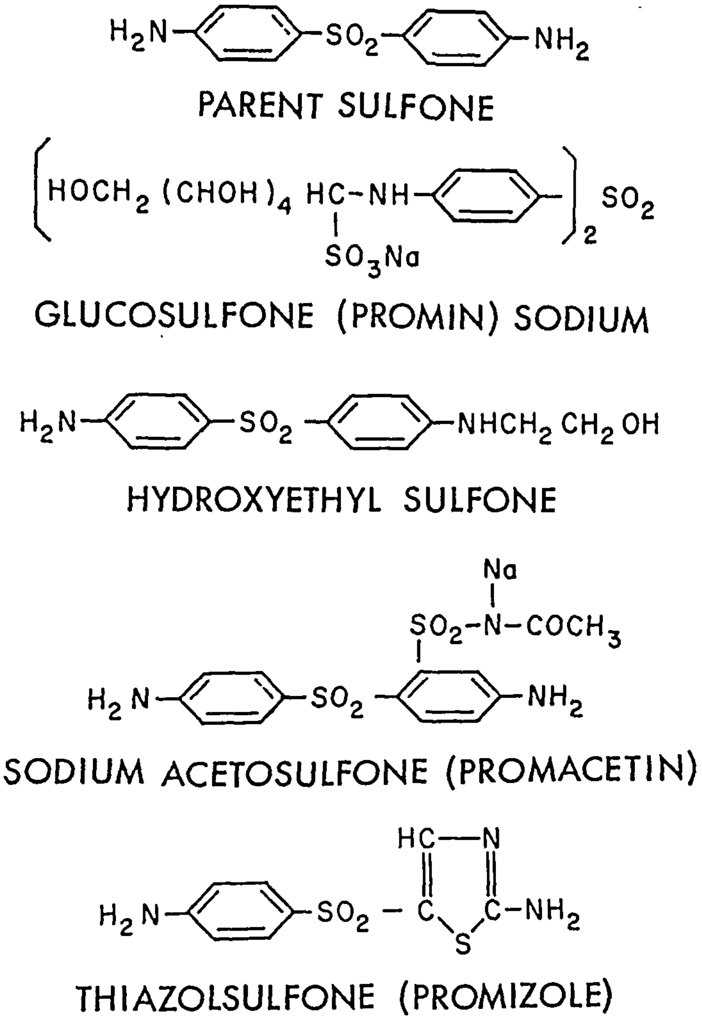
From the Medical Department of the Leonard Wood Memorial (American Leprosy Foundation).

fon, Tisin, Tyvid), but it has led to the successful use of the sulfones, streptomycin, and certain diphenyl thioureas in leprosy in humans.

In the preparation of this paper, liberal use has been made of recent reviews, especially those of Bushby,[1] Buu-Hoi,[2] Lechat,[3] and Sharp and Payne.[4] The description of the chemical structure of the sulfones, their pharmacology, toxicity, inhibitory capacity, and effectiveness in experimental infections (see figure) are slightly modified from those of Chang, Wolcott, and Doull.[5]


PARENT SULFONE
GLUCOSULFONE (PROMIN) SODIUM
HYDROXYETHYL SULFONE
SODIUM ACETOSULFONE (PROMACETIN)
THIAZOLSULFONE (PROMIZOLE)

Chemical structures of various sulfone compounds.

Incidence of Leprosy

Leprosy is an uncommon disease in the continental United States, the known prevalence being fewer than 1,000 cases. It occurs indigenously at a low level in southeastern Texas, still lower in Louisiana, and rarely in southern California and Florida (Key West). Occasional cases are detected among immigrants from areas in which the disease is endemic and among missionaries, educators, veterans of the military services, and others who have lived temporarily in such areas. When the known cases in Hawaii, Puerto Rico, and American Samoa are added, the total count is still well below 2,000. Despite its low prevalence in the United States, leprosy excites the interest of American physicians because of its unique history, the complexity of its clinical syndrome, its great public health importance in many countries—the world total being estimated at 10 million—and the challenge which its unsolved problems offer to science.

Classification of Types of Leprosy

Although leprosy is a generalized infection, the more manifest lesions are those of the skin, the mucous membranes of the upper respiratory tract, and certain peripheral nerves. In 1848, Danielssen and Boeck,[6] the Norwegian pioneers, described two principal clinical forms, tuberous (nodular) and anesthetic. In 1894, Hansen and Looft[7] changed the latter name to maculoanesthetic. This exclusively clinical classification was dominant for many years, although the nodular type became known as cutaneous and later as lepromatous, and the maculoanesthetic type was often called neural. The division was a useful one, but, since damage to peripheral nerve trunks and its sequelae occurred sooner or later in the nodular (cutaneous) type, many cases were thrown into a third category (no longer valid) called "mixed leprosy." This terminology was unsatisfactory, but further knowledge was required before classification could be put on a sounder basis.

Developments came on three fronts. With increasing study of the clinical varieties in different parts of the world, it became evident that there were cases which had been classed as nodular or cutaneous that were, in fact, different from the usual lepromatous ones. These had clearly delimited, erythematous nodulations or plaques which tended to progress peripherally and to resolve centrally, with central anesthesia. It also became evident that maculoanesthetic cases having anesthetic macules, with elevated, slowly progressing margins, were related to them. Histologically, it was demonstrated that these lesions all showed a characteristic tuberculoid structure and not the well-known lepromatous picture. The introduction of the lepromin (Mitsuda-Hayashi) test, which consists of the intradermal injection of a suspension of heat-killed, bacillus-rich, lepromatous tissue, was another important event. This test almost always caused reactions in patients showing these varieties of anesthetic plaques and macules; in the classical and more severe lepromatous type, the reaction was negative, suggesting that the form of disease which developed in the infected person depended primarily on tissue reactivity, signifying the presence or absence of resistance. These observations—clinical, histological, and immunological—provided a basis for a more satisfactory classification.

As the culmination of acts of several preceding international conferences since 1930, the Sixth International Congress of Leprology held at Madrid in 1953 adopted the present "official" classification scheme with definitions of two major (polar) types, lepromatous and tuberculoid, and of two supplementary classes or groups, borderline (cases between the two types) and indeterminate (cases with *simple* macular lesions).

Lepromatous cases are the most serious and most infectious, Myco. leprae being readily demonstrable in smears from the skin lesions and the nasal mucosa of patients. The lepromin reaction is negative. More or less extensive thickening of the skin is always present in well-established cases, and definite nodulation occurs with varying frequency. The borders of the lepromatous infiltrations are ill-defined. There may or may not be definite disturbance of sensation within the area of the lesion. The histological structure observed in the skin is granulomatous in nature, typically with Virchow cells (bacillus-laden histiocytes) which tend to become foamy as they age. As the disease progresses, the larger nerve trunks are invaded, especially the ulnars and peroneals. Anesthesia, atrophy of skin and muscle, absorption of the small bones of the hands and feet, ulceration, and natural amputation then follow; the ultimate destruction is equal to the worst that may be seen in the tuberculoid type of leprosy.

In the tuberculoid type, the characteristic macules have well-defined, more or less elevated margins, showing clearing at the center. The surface is often papillated. Anesthesia is invariably present within these lesions. The lepromin reaction is usually positive. Myco. leprae is rarely demonstrable in smears from the quiescent lesions but may be present in considerable numbers in the larger tuberculoid ones during reactive phases. The histological structure is also granulomatous, but there are no Virchow cells. The predominant cells are epithelioid, which form noncaseating foci, and giant cells of the Langhans type are frequent. The reactional lesions may sometimes invade the epidermis. The earliest signs ordinarily are macules, but sometimes the distal effects of invasion of nerve trunks are more conspicuous, such as contractures of the fingers and toes, wasting of the interossei, and anesthesia. At a later stage, the neural sequelae are the same as those described for the lepromatous type.

Probably because of greater interest in recent years, borderline cases, previously classified as lepromatous, are being reported with increasing frequency. Plaques may show histological features of both polar types, but the tuberculoid picture, often atypical, predominates. Mainly, it is the mixed clinical picture which determines a diagnosis of this class. Smears are positive for bacilli, and the lepromin reaction is usually negative. These cases usually arise from tuberculoid ones as a result of repeated reactions, and they may become frankly lepromatous.

In the indeterminate class, the lesions are simple, flat macules which show some disturbance of sensation; smears may reveal small numbers of Myco. leprae. The lepromin reaction may be positive or negative. The histological findings are those of simple, chronic inflammation. These cases are capable of progression toward either the lepromatous or the tuberculoid type.

Clinical Evaluation Studies of Leonard Wood Memorial

The nature of leprosy makes it essential that therapeutic trials be adequately controlled; otherwise, drugs that have value but fall short of complete success may pass undetected and be discarded. Most emphasis has been placed on severe and advanced disease, but all gradations of lesions can be recognized from the small macules (which may disappear spontaneously) to the far-advanced nodulation of the lepromatous type. The course of leprosy is prolonged over many years, with a tendency towards arrest of the active process, but there may be many exacerbations and remissions. Clinical impressions of the value of any therapeutic procedure may, therefore, be erroneous. The density of acid-fast bacilli in the skin also is an uncertain guide; reduction occurs frequently in the course of time without specific treatment, and there is no reliable method of distinguishing between the living and multiplying bacilli and those that are dead.

In 1941, in the earliest trials of the sulfones for the treatment of leprosy, a small, controlled study was carried out by Faget and his associates[8] at the Public Health Service Hospital (National Leprosarium), Carville, La. In 1951, large scale studies of longer duration were commenced by the Leonard Wood Memorial in cooperation with leprosariums in Japan, the Philippines, and the Union of South Africa, with financial aid from the Public Health Service and several pharmaceutical manufacturers. Three series have been completed,[9] and the trials are still going on. Reference is made later to the results obtained with various drugs, but certain general features may be mentioned.

The recognized principles of controlled clinical trials have been adhered to as closely as possible. Identical experiments have been conducted in at least two widely separated institutions. Only patients with the lepromatous type of the disease have been included, and patients have been assigned to therapy groups at random by statisticians in the United States. The groups have always been closely comparable to one another in such background items as age, sex, prior therapy, and current clinical and bacteriological status. Nevertheless, after eight years of study, we still do not know whether the age or sex of the patient has any significant bearing on response to therapy, although we continue to take these factors into account. A more disconcerting fact is that we have been unable to demonstrate greater clinical progress with identical treatment in less advanced cases than in those in whom the disease was well established at the commencement of therapy. This is probably a reflection of the slowness of clinical improvement and of the difficulty in demonstrating improvement in lesions that are slight at the beginning. Bacteriological measurements have likewise been inadequate to indicate any significance which age, sex, and stage of disease may have on prognosis.

The double-blind type of experiment was applied in our fourth series, which was continued for two years. There were four groups in this experiment. Two groups were treated with sulfones which were readily detectable in the blood. (It was necessary to obtain agreement from the clinicians and consultants not to consult the laboratory records.) Patients who became worse were withdrawn from the study and were referred to a special consultant not connected with the tests, who was told in confidence the treatment that had been given in order that he might treat the patient rationally. An unexpected complication arose which identified one of the drugs and forced its discontinuance at the end of one and one-half years. This was the occurrence of blueness (still inadequately explained) in the lesions of patients treated with amodiaquine (Camoquin) hydrochloride. The agents used in the other three groups remained unidentified to the end of the two-year period.

Another troublesome feature in these trials was the failure of a substantial proportion of the patients (10 to 20%) to complete the prescribed courses of treatment. This occurs to a greater or lesser extent in all long-term studies. Fatalities were few. The chief reason for discontinuance of therapy was the overwhelming desire of some of the patients to leave the institution against medical advice. In every instance, the patient's reasons were examined critically to make certain that they were not related to improvement or worsening of the disease or to the side-effects of a drug. Ultimately, the best that we can do is to study the comparability of the groups when the study ends, with respect to background factors that are definite, measurable, and that were more or less equal at the outset.

Older Forms of Therapy

Chaulmoogra Oil.—The history of the treatment of leprosy with chaulmoogra (Hydnocarpus) oil is an illuminative example of the necessity for adequately controlled studies of therapies. For generations, this oil was the popular remedy, and its esters and other derivatives were in world-wide use for almost twenty-five years. Hundreds of favorable case reports appeared, with photographs taken before and after treatment and with imposing statistics of arrest of the disease. In 1930, a publication[10] from the National Leprosarium gave case reports for 65 recoveries, but these were credited to a variety of factors, in addition to specific treatment with chaulmoogra oil and its esters. Johansen and Erickson[11] reported that, in 1926, experienced leprologists at that hospital considered that definite improvement had followed the use of the oil or its esters in a sufficiently large percentage of cases to warrant continuation of the treatment. By 1938, improvement was still noted, "although a considerable number of the older advanced cases show retrogression."[11] In 1942, the impression persisted that the chaulmoogra oil products were of some benefit. By 1946, after chaulmoogra oil was used for five years along with the sulfones, the popularity of chaulmoogra preparations had declined, but they were still being used in certain types of cases. In 1947, their use was entirely abandoned at the National Leprosarium. At present, chaulmoogra oil is used at only a few centers, usually as a supplement to a sulfone. A treatment that had attained universal popularity among leprologists and patients alike has been relegated to the shelves of the historical library; its value remains uncertain because controlled studies were not made.

Metals.—Several antimony, arsenic, bismuth, mercurial, and gold compounds have been tried in leprosy, usually with detrimental results. Small doses of potassium iodide have also been used ineffectively by a number of leprologists. Merbromin (Mercurochrome) was subjected to an extensive trial at the National Leprosarium during the period from 1924 to 1925.[10] It was reported to be of value in checking rapid retrogression and in treatment of lepromatous ulcers. Antimony is still used in treatment of "reactions."

Dyes.—Various aniline and other dyes have been used therapeutically by intravenous injection (methylene blue, trypan blue, and fluorescein). The end-results were disappointing. Certain of these dyes have an affinity for lepromatous lesions, and, in cases of the borderline class of lesions, methylene blue has been used to differentiate such lesions from those of tuberculoid structure.

Sulfones

Although *p,p'*-sulfonyldianiline (DDS) was synthesized in 1908 by Fromm and Wittmann during their research on chemical dyes, it was not until 1937, after the phenomenal effectiveness of sulfonamides had been demonstrated, that this compound was tried against infections in laboratory animals. It proved to be far superior to sulfanilamide in streptococcic infections in mice but was much more toxic. In 1938, according to reports published more than 10 years later, it was used in man in doses of 1 to 2 Gm. daily for the treatment of acute streptococcic infections; however, it caused severe hemolytic anemia, and use of this agent was abandoned.

In 1939, Rist[12] of the Pasteur Institute found that DDS had a much stronger bacteriostatic (in vitro) effect than did a sulfanilamide against both human and avian types of the tubercle bacillus, and, in the same year, Rist, Bloch, and Hamon[13] reported favorable results with experimental infection of the avian type in the rabbit. Probably because of the toxicity observed in animals, these reports did not lead immediately to the trial of DDS as a therapeutic agent in either tuberculosis or leprosy.

In 1937, Tilletson and colleagues, starting with DDS, prepared a soluble and less toxic compound, glucosulfone (Promin) sodium. During the next two years, the effect of glucosulfone was studied in several infections, but the results were not spectacular. It was toxic when given orally, even in small doses, irritating when injected subcutaneously, but well tolerated when given intravenously.

The discovery of glucosulfone led to the use of sulfones in leprosy. The intervening and significant event was the publication on Oct. 30, 1940, by Feldman, Hinshaw, and Moses[14] at the Mayo Foundation, of favorable results with the drug in experimental tuberculosis in the guinea pig. This report came to the attention of Dr. G. H. Faget of the National Leprosarium who obtained a supply of the drug. In March of 1941, the first patients were treated in a study which eventually revolutionized the treatment of leprosy.[8]

In the sulfone compounds, the sulfonyl radical, $R\text{-}SO_2\text{-}R$, is combined with two carbon atoms, whereas in the sulfonamides, this radical, $R\text{-}SO_2\text{-}NH_2$, is combined with one carbon atom and an amino group. The principal sulfones which have been used therapeutically may be classified as follows: (1) parent sulfone, *p,p′*-sulfonyldianiline (DDS); (2) disubstituted derivatives having a substituent in each amino group such as glucosulfone sodium (*p,p′*-diaminodiphenylsulfone-N,N′-di-[dextrose sodium sulfonate]), and other examples: sulfoxone (Diasone) sodium, solapsone (Sulphetrone), Hydnosulphone; (3) monosubstituted compounds having one free amino group such as hydroxyethyl sulfone (4-amino-4′-hydroxyethylaminodiphenyl sulfone), and other examples: succinylsulfone, Exosulfonyl (succinylamido-4-amino-4′-diphenyl sulfone), Succisulphone, or 1500F, and phenylglycine sulfone or sulfone Cilag; (4) nuclearsubstituted derivatives with two free amino groups such as sodium acetosulfone (Promacetin or Internal Antiseptic no. 307 [sodium 4,4′-diaminodiphenylsulfone-2-*N*-acetylsulfonamide]), and propiosulfone (sodium 4,4′-diaminodiphenyl sulfone-2-sulfono-propionamide); and (5) asymmetric sulfone with two free amino groups such as thiazolsulfone (Promizole) (2-amino-5-sulfanilylthiazole). The chemical structures for examples of these compounds are given in the figure.

Pharmacology.—After usual therapeutic doses, the sulfones may be found in all body tissues and fluids. The liver and kidneys contain relatively high concentrations. The approximate blood levels reached with therapeutic doses are: DDS and hydroxyethyl sulfone, 0.5 mg. per 100 cc.; sulfoxone sodium, succinylsulfone, and sodium acetosulfone, 1 to 1.5 mg.; and glucosulfone sodium and solapsone, 4 to 5 mg. These levels increase, roughly, with molecular weights.

Individual variations in absorption and excretion occur after oral administration among patients taking the same dosage. In general, DDS is considered to be completely absorbed, because 90% of the oral intake is found in the urine, and only a trace is detectable in the feces. Sulfoxone is about 50% absorbed; 48% has been found in the urine and 44% in the feces. Solapsone is poorly absorbed; 10% is found in the urine and up to 80% in the feces. Acetosulfone is likewise poorly absorbed; 25% is excreted in the urine, and a large proportion is passed in the feces. Thiazolsulfone is well absorbed and rapidly eliminated. As high as 800 mg. per 100 cc. has been found in the urine of patients taking 6 to 7 Gm. daily by mouth. The urine may become pink to cherry red in color. About 50% of monosubstituted compounds is excreted in the urine.

After parenteral administration, from 95 to 100% of glucosulfone is excreted in the urine. Blood levels drop rapidly, especially in the first two hours after administration, but, after a dosage of 2 Gm. or more, appreciable levels are present after eight hours.

Disubstituted compounds are usually retained in measurable quantities in the patient's blood for about 14 days after cessation of treatment and, sometimes, even for four weeks or longer. DDS is even more cumulative, especially after parenteral administration. The high concentration of sulfones in the bile is of interest because biliary excretion and reabsorption tend to prolong retention and may be responsible for sulfones occasionally being found in the blood or urine long after cessation of treatment. Regular rest periods during therapy are, therefore, advisable. Because of cumulation, sulfones administered in moderate doses once or twice a week have been found to give blood levels more or less equal to those attained by administration of smaller daily doses.

There has been discussion of the hypothesis that the action of disubstituted sulfones is attributable chiefly to liberation of DDS in the body. The toxicity of glucosulfone, when given orally, is thought to be caused by breakdown to DDS in the gastrointestinal tract, and high concentrations of free DDS have been found in the blood and urine of patients treated with other disubstituted compounds given by the oral route. When given parenterally, glucosulfone and solapsone present a different picture. Only small amounts of free DDS are found in the blood and urine. Monosubstituted (hydroxyethyl sulfone) and nuclear-substituted derivatives (acetosulfone) do not break down to DDS; they act as entire molecules.

Toxicity for Animals.—Given orally, DDS is 5 to 7 times as toxic for mice as is glucosulfone, 8 to 12 times as toxic as sulfoxone, and more than 30 times as toxic as solapsone and acetosulfone. Excitement is a prominent sign resulting from treatment with DDS. Mice maintained on such therapy often run continuously around in their cages, and, if released, will run off the table. Larger doses cause various degrees of paralysis, including difficulty in respiration. Cyanosis is common in domestic animals. In sheep, and less severely in dogs and goats, excitement, nervous nodding, twitching of the lips, and pyrexia are seen. These may be followed by convulsions and paraplegia. No involvement of the nervous system has been observed in cattle even after large doses. Hemolytic anemia has been reported in guinea pigs given glucosulfone and in rabbits after administration of solapsone. Direct destruction of mature erythrocytes is considered to be the cause; a more remote suggestion is that sulfones inhibit intestinal bacterial flora, thus interfering with synthesis of the vitamin B complex and causing a deficiency anemia. Studies on chronic toxicity caused by various sulfones in rats, guinea pigs, and cats indicate that solapsone and hydroxyethyl sulfone are the least toxic.

Inhibitory Capacity Against Mycobacteria.—Because of inability to cultivate Myco. leprae in vitro, opinions on bacteriostatic capacity are based on effect on other species of mycobacteria; most work has been done on Myco. tuberculosis. DDS was shown to be active against the avian type of tubercle bacillus as early as 1939. The sulfone with the highest bacteriostatic power against the human type of tubercle bacillus is DDS, which is about twice as active as hydroxyethyl sulfone and 10 to 25 times as active as glucosulfone. Para-aminobenzoic acid is antagonistic and is known to inhibit, in whole or in part, the action of glucosulfone against Myco. tuberculosis and the action of DDS against Diplococcus pneumoniae.

Effectiveness in Experimental Tuberculosis.—In addition to DDS and glucosulfone, hydroxyethyl sulfone has been found to delay death in guinea pigs infected with Myco. tuberculosis. Sulfoxone, solapsone, and phenylglycine sulfone are only slightly active in this respect, and acetosulfone is inactive. Evidence of synergistic effect has been obtained with combinations of streptomycin and various sulfones.

Effectiveness in Other Mycobacterial Infections.—The ulcerative skin disease of man caused by Myco. ulcerans is transmissible to rats and mice. Both DDS and streptomycin are markedly effective in repressing the experimental disease in mice. The disease of rats and mice caused by Myco. lepraemurium resembles human leprosy somewhat, but the peripheral nerves are not involved. The bacillus has not been cultivated in vitro. A number of sulfones and certain other drugs have been shown to exert repressive action in the experimental disease, but none has prevented death. In the mycobacterial enteritis of cattle and sheep known as Johne's disease, the sulfones are ineffective.

Clinical Use in Leprosy.—The trial of glucosulfone sodium at the National Leprosarium followed by only a few months a disappointing experience with sulfanilamide.[8] This drug cleared up secondary infections in certain cases, but it had no observable effect on leprous lesions after about three months. Toxic complications were thought to be more frequent and severe than those found in other infectious diseases after administration of sulfanilamide. Glucosulfone, likewise, was toxic when given orally to 10 patients, in doses of 500 mg. to 1 Gm. daily. Severe hemolysis occurred in some patients. Intravenous administration, however, was well tolerated—as had been the experience in other diseases. Moderate degrees of anemia continued to be frequent but were treated successfully with administration of inorganic iron. After 12 months of treatment with glucosulfone, the disease in 15 of the 22 patients had improved; in 6, it was stationary, and in 1, worse. Five patients had tested negative bacteriologically. Ulceration of the nasal septum was seen to heal, and there was improvement in laryngitis and in ease of respiration. In several patients attending the dental clinic, the lesions of the lips and of the soft and hard palate had healed.

Since it was recognized that spontaneous improvement may have played a part, the small controlled experiment, previously mentioned,[8] was carried out. Acetosulfone was given to 20 patients in oral doses of 300 mg. to 1 Gm. daily. The same number of patients, matched as to type and stage of disease, were given a placebo. After eight months, the condition of the acetosulfone-treated group was superior to the other, especially in regard to such complications as rhinitis, laryngitis, and lepromatous ulceration of the skin.

The search for sulfone compounds which could be given orally eventually yielded a considerable number. The first to be used extensively was sulfoxone sodium; this was first used by Muir[15] in Trinidad. Solapsone was produced a little later and also came into extensive use. Acetosulfone, thiazolsulfone, and several other compounds gave favorable results in early trials, but cost of production limited their use.

In 1947, Cochrane and associates[16] in India, on learning that mastitis of cattle was being treated with injections of DDS, the parent sulfone of all aforementioned derivatives, obtained a 25% suspension of DDS in peanut oil. This was given by subcutaneous injection to a small group of patients in a dosage of 5 cc. (1.25 Gm. of DDS) twice weekly. Severe anemia occurred in several patients and psychosis in a few, but there was no evidence of hepatitis. Shortly afterward, Lowe and Smith[17] administered DDS by the oral route in much smaller doses; there was little evidence of toxicity, and the treatment appeared to be effective. In recent years, DDS has largely replaced other sulfone compounds in the treatment of leprosy, chiefly because of its low cost. Many leprologists, especially those working in outpatient clinics in Africa, prefer to administer therapy by the parenteral route. There is no convincing evidence that the mode of administration of DDS influences its effectiveness or the frequency of erythema nodosum or other reactions of lepromatous leprosy.

Effectiveness of Sulfones.—It is only in the lepromatous variety that adequately controlled studies have been made, although the great majority of reports indicate good results in the cutaneous lesions of the tuberculoid type. In the lepromatous type, DDS has been shown to be equal to sulfoxone in studies lasting 48 weeks conducted by the Leonard Wood Memorial, and this conclusion can probably be extended to solapsone and other disubstituted compounds.

The greatest improvement observed in patients during sulfone therapy occurs in ulcerative lepromatous lesions of the skin and mucosa. Nasal obstruction, hoarseness, and other signs of involvement of the upper air passages are usually greatly improved within three to six months. Tracheotomy, which was formerly a common operation in large leprosariums, has become rare. Lepromatous ulceration of the skin heals fairly promptly, and, consequently, there has been a marked reduction in the use of bandages. Improvement in diffuse infiltration of the skin and disappearance of plaques and nodules take place much more slowly. Clinical improvement is not accompanied by characteristic histological changes. The histological picture becomes predominantly atrophic, resembling that which occurs in spontaneous remission, without treatment of any sort. The explanation may be that the sulfones eliminate bacilli from the blood vessels and blood stream, thereby preventing formation of new lesions and permitting natural recovery to take place. Cystic lesions of the bones of the hands and feet, presumably due to invasion by Myco. leprae, have improved with sulfone therapy.

Invasion of peripheral nerves probably occurs in all cases of leprosy; there is one school of leprology which teaches that the spread of the bacilli, on entrance through the skin, takes place along the fine fibers of the cutaneous nerves. In the tuberculoid type, the neural elements in the dermis are completely destroyed. The explanation is not clear because usually no bacilli, or rare ones, can be demonstrated. In the lepromatous type, however, there are many bacilli, and the destruction of nerve fibers may be explained by pressure from growth of lepromatous tissue. In both types, but particularly in the tuberculoid type, the enlargement of the ulnar, peroneal, and posterior occipital nerve trunks may be conspicuous. Repeated and extremely painful attacks of neuritis are common—especially of the ulnar. In this instance, splinting the arm and keeping it warm are always advisable. Nerve stripping has been advocated to relieve pain, but this is not of permanent value. Local injections of cortisone (Cortisone, Cortogen, Cortone) acetate and procaine hydrochloride, with or without hyaluronidase (Alidase, Diffusin, Hyazyme, Wydase), may be of value in lessening nerve destruction, if given when acute neuritis first appears.

By the time that many patients seek treatment, destruction of nerves has taken place. Contractures, atrophy of skin and muscles, extensive anesthesia (often of the glove and stocking distribution), perforating ulcer of the foot, and some absorption of the small bones of the hands and feet may already be present. These changes are irreversible, although transplantation of tendons and other surgical procedures, together with physiotherapy, can do much to restore function. The question as to whether sulfone therapy can prevent or limit nerve damage and its sequelae is of vital importance but is as yet unanswered.

Bacteriological negativity, as judged from microscopic examination of simple smears from the skin, is slowly attained. After one year of therapy, about 90% of patients still have positive smears, and, after five years of treatment, 40 or 50% may still have positive smear tests. Bacteriological improvement, however, is demonstrable in a high proportion after one year. Smears from the nasal septum improve but do not become negative as rapidly as was formerly thought. Septal ulcers become clean but often do not entirely heal and may continue to discharge bacilli in diminished numbers. In the first series of the studies of the Leonard Wood Memorial, in groups of sulfone-treated patients, bacteriological improvement was greater for nasal septum sites than for skin sites after 16 weeks and after 32 weeks of therapy, but this finding has not been consistent in our subsequent work.

Bacteriological improvement, even if short of negativity, may be of great public health significance. Rapid increases in prevalence of leprosy are rare; in fact, the disease usually appears to have difficulty in maintaining itself, and it has disappeared from many areas where it once was prevalent. The biological balance between man and the leprosy bacillus is a nearly even one—with a slight advantage for man. A substantial reduction in the output of bacilli, therefore, rather than total negativity of the patient, may be all that is required to initiate or accelerate decline of the disease.

The recommended dosages of the sulfones in common use are given in the table.

Toxicity and Side-Effects.—The sulfones have a high safety record. At Carville, La., more than 1,100 patients have taken one or another compound for prolonged periods without a single instance of fatality or serious illness attributable to the drug. This does not mean that sulfones and particularly DDS can be used indiscriminately, without medical supervision. In outpatient treatment of large numbers of patients in Nigeria and the Belgian Congo, a few fatalities have been attributed to administration of DDS. Jaundice has usually been present, and, while the fatalities may have been due to the drug, other causes of hepatitis have not been excluded. One fatal case of granulocytopenia has recently been reported after treatment of a patient for dermatitis herpetiformis with DDS.

The most commonly reported toxic effect is hemolytic anemia. In some cases, there has been confusion with anemias caused by malnutrition, intestinal parasites, and by uncomplicated leprosy. Secondary anemias caused by sulfones may be corrected by administration of ferrous salts alone or supplemented by liver extracts. Sometimes it is advisable to lower the dosage of sulfones for a few weeks, but it is rarely necessary to discontinue treatment.

Recommended Dosages of Principal Sulfones in Current Use

		Mg./Kg. of Body Weight		
Drug	Route	Initial	Maximum*	Frequency†
DDS	Oral	0.5	3.0	Daily
DDS	Parenteral	1.0	8.0	Twice weekly
Sulfoxone sodium	Oral	3.0	20.0	Daily
Glucosulfone sodium	Intravenous	20.0	100.0	Daily
Solapsone	Oral	20.0	120.0	Daily
Solapsone	Intramuscular	5.0	30.0	Twice weekly

* Attained after an induction period of 6 to 8 weeks.

† In many institutions, daily doses are omitted on Sundays. For all preparations, rest periods of two weeks should alternate with therapy periods of three months.

Dermatitis, in a variety of forms, may occur. When this happens, treatment should be discontinued. Sometimes another sulfone is well tolerated after the rash disappears.

The urinary tract is remarkably tolerant to the sulfones. Patients who have albuminuria, however, may not be able to take full dosage and should be kept under close observation. Amyloid nephrosis has long been recognized as a leading cause of death at the National Leprosarium, but, for some unknown reason, it does not seem to be as common in foreign leprosariums. Advanced amyloidosis of the kidneys is a part of generalized amyloidosis and is a contraindication to sulfone therapy.

Relapses.—Relapses may occur in lepromatous leprosy after long and intensive sulfone treatment. It is probable that these relapses are lessened in frequency by continuation of treatment, but this has not been demonstrated. Permanent cure can never be assured, and it is recommended that patients whose disease is apparently arrested should continue on a low dosage of a sulfone for life.

Other Drugs

Sodium aminosalicylate (Pamisyl Sodium, Para-Pas Sodium, Parasal Sodium, Pasara Sodium, Pasem Sodium, Pasmed Sodium, Sodium *p*-Aminosalicylate, Sodium Para-Aminosalicylate) was tested against leprosy at the Westfort Institution, Pretoria, South Africa, during one of the clinical trials by the Leonard Wood Memorial. It was considered to have some activity and should be subjected to more extensive study.

Thioureas (Thiocarbamides).—After favorable reports by others, the Leonard Wood Memorial tested the value in lepromatous leprosy of a disubstituted thiourea, thiocarbanilide (4-butoxy-4′-dimethylaminodiphenyl thiourea). The trial was a controlled one, conducted over a two-year period in exactly the same pattern at each of two Philippine institutions. The drug was given in a daily dosage of 60 mg. per kilogram of body weight. There were three other therapy groups in the experiment, given, respectively, amodiaquine hydrochloride, 200 mg. daily; DDS, 4 mg. per kilogram of body weight; and DDS, 2.5 mg. per kilogram of body weight. After 72 weeks, the amodiaquine was withdrawn because it was clearly inferior to the other drugs. The thiourea appeared to be slightly inferior to DDS, but the only difference which was significant statistically was lesser improvement in the smears from the nasal septum. After 96 weeks, the clinical and bacteriological results at each institution both pointed to lesser value of the thiourea, and, when the data for both institutions were combined, this finding was definitely indicated. Nevertheless, the drug caused no toxicity and showed up well in this rigid test. Therefore, its use should be considered whenever sulfones are ineffective or not well tolerated. Buu-Hoi[2] has reported good results with another thiourea, 4,4′-diethoxycarbanilide (Dialid).

The thiosemicarbazones may be regarded as monosubstituted thioureas. One of these, amithiozone (Benthiozon, Conteben, Tibione), which has had rather a wide trial in treatment of tuberculosis, has been used in the treatment of leprosy by a number of workers. Early results were promising, but this was generally not true of the second and third years of treatment. In those instances in which clinical improvement continued to occur over a period of three years, attainment of bacteriological negativity was rare. Also, there were instances of serious toxic effects, including granulocytopenia, allergic dermatitis, and recurrent drug fever.

Mercaptan Compounds.—Certain mercaptan compounds have shown antituberculosis activity in mice, which has led to clinical trials in leprosy. The mercaptans or thioalcohols are mostly colorless volatile liquids with the odor of garlic, the elimination of which is still a problem. The activity is supposed to be due to liberation of ethyl mercaptan. In the treatment of leprosy, two preparations have been used: (1) sodium ethyl thiosulfate (ET) given as pills in a dosage of 1.2 Gm. daily and (2) diethyl dithiolisophthalate (ETIP, Etisul) given by inunction in a dosage of 5 Gm. three times a week. Preliminary reports have been favorable, and larger and more adequately controlled trials are contemplated.

Nicotinic Acid Derivatives.—Nicotinamide, in a maximum dosage for adults of 500 mg. daily, was given as a supplement to DDS in clinical trials carried out in an identical pattern at each of three leprosariums, two in the Philippines and one in the Union of South Africa. A reference group was treated with DDS. The nicotinamide group showed no advantage at the end of 48 weeks.

Isoniazid was tried by many leprologists after favorable reports, in 1952, of its value in tuberculosis. The reports are not all in agreement, but the consensus is that this drug is less effective than DDS. In a large-scale study (second series) of the Leonard Wood Memorial, isoniazid was used as a supplement to sulfoxone, but no additive effect was observed by the end of 48 weeks. It was also used in a small number of patients in combination with pyrazinamide, but the results were no better than those observed in a reference group treated with DDS.

Isonicotinylhydrazone of 2-formyl-phenoxyacetic acid (Compound 377), which has a markedly repressive action in experimental tuberculosis in mice, was used in patients with lepromatous leprosy in a controlled study at the Westfort Institution, Union of South Africa, in a maximum dosage of 900 mg. per day. At the end of 72 weeks, patients treated with DDS showed somewhat greater improvement than those given Compound 377, as judged by both clinical and bacteriological standards.

Antibiotics

Streptomycin and Dihydrostreptomycin.—Streptomycin was first used in the treatment of leprosy in 1946, at the National Leprosarium.[11] The dosage was 2 Gm. daily given in eight divided doses, for four months. Improvement was noted especially in lesions of the mucous membranes of the upper respiratory tract, but toxic effects were severe and frequent. In the first series of the Clinical Evaluation Studies of the Leonard Wood Memorial, already mentioned, dihydrostreptomycin sulfate was given in a dosage of 1 Gm. three times a week to three groups treated, respectively, with dihydrostreptomycin alone, dihydrostreptomycin in combination with sulfoxone, and dihydrostreptomycin in combination with sodium aminosalicylate. A fourth group received sulfoxone alone; a fifth, DDS; and a sixth, the control group, received a placebo (in Japan and the Philippines) and sodium aminosalicylate (in South Africa). Clinical improvement occurred in about the same proportion of all groups at each center, except the one which was given the placebo at the Japanese and Philippine institutions. Bacteriological improvement occurred in all groups, including the controls, at all centers. It was concluded that sulfoxone, DDS, and dihydrostreptomycin were of definite and of equal value so far as judgment could be made after 48 weeks of therapy. The results were disappointing in that combined treatment with sulfoxone and dihydrostreptomycin, or with dihydrostreptomycin and sodium aminosalicylate, offered no additive advantage over sulfoxone, DDS, or dihydrostreptomycin given alone.

In the second series of the Memorial's studies, dihydrostreptomycin was used in combination with isoniazid. Dihydrostreptomycin was given twice weekly in a dosage of 1 Gm., and isoniazid was given in a daily dosage of 10 mg. per kilogram of body weight. At the end of 48 weeks, this combination showed no advantage over sulfoxone used alone.

Penicillin.—Penicillin has been tried in leprosy at a number of centers, beginning in 1944, in doses which have varied from 25,000 units daily to 100,000 units. Massive doses have not been used. Treatment has been continued for varying periods, with a beneficial effect on the healing of nonleprous ulcers but with no effect on Myco. leprae or on the course of the disease.

Cycloserine (Seromycin).—Cycloserine has been used in several studies. In small, matched groups of lepromatous patients at two Philippine leprosariums, treated respectively with cycloserine and DDS for 48 weeks, the antibiotic showed some therapeutic action, but there was no evidence of superiority over the sulfones. Cycloserine was well tolerated by these patients.

Other antibiotics have received limited trials, and a positive statement regarding them cannot be made. Chlortetracycline (Aureomycin) hydrochloride showed good results in a small series at Carville, La., and chloramphenicol (Chloromycetin) gave negative results in a few cases in Cuba.

Nonspecific Vaccine Therapy

The opinion that natural reactivity to lepromin indicates some degree of resistance to leprosy has led to attempts to induce reactivity in lepromatous patients by artificial means. Acquirement of reactivity, associated with clinical and bacteriological improvement, has been reported to follow vaccination with a vaccine prepared from killed Myco. marinum, which was originally isolated from a leprous nodule. This series was uncontrolled, and the results have not been confirmed by others. Tuberculosis (BCG) vaccine has been used by a number of leprologists. In the third series of the studies of the Leonard Wood Memorial, repeated vaccinations with this vaccine did not induce reactivity in a significant proportion of the patients and had no effect on the course of lepromatous leprosy.

Treatment of Complications

Lesions of Eye.—In lepromatous leprosy, the bacilli lodge in the anterior segment of the eye, but the path of invasion is unknown. Nodules may appear in the conjunctiva and episclera. A type of superficial punctate keratitis marked by discrete interstitial opacities, without pain or disturbance of vision, is considered to be pathognomonic of leprosy. Ulceration of the cornea, pannus formation, and a sclerotic keratitis follow. The iris and ciliary body are usually affected, and chronic plastic iridocyclitis is the principal cause of blindness. Acute iridocyclitis is often associated with an attack of erythema nodosum.

The opinion is widely held by leprologists that sulfone therapy will prevent ocular leprosy or limit its progress. In the cooperative studies of the Leonard Wood Memorial, keratoconjunctivitis has cleared up with sulfone therapy, but new instances have also occurred. Further study of this important aspect of therapy is necessary. Cortisone is effective in the acute exacerbations of iridocyclitis and iritis. At the National Leprosarium, local applications have been useful. The consulting ophthalmologist, Dr. James H. Allen of New Orleans, uses cortisone acetate in a strength of 0.5%. Remission is only temporary, but the treatment appears to be equally effective in recurrences of the acute process. Whether lepromatous keratitis and iridocyclitis can be controlled indefinitely remains to be proved, but, in the meantime, pain is relieved, and possession of useful sight is prolonged.

In both the lepromatous and tuberculoid types, eye lesions may be secondary to nerve involvement. Anesthesia of the conjunctiva and cornea follows involvement of the ophthalmic division of the fifth cranial nerve. Unnoticed injury and painless corneal ulceration may ensue. Lagophthalmos follows damage to the temporal and zygomatic branches of the seventh nerve, and exposure keratitis may develop. Considering the frequency with which one or both of these nerves are involved, especially in the tuberculoid type, the number of patients who lose their sight in this manner is surprisingly small. Nevertheless, the advantages of tarsorrhaphy should always be considered.

Reactions During Therapy.—Repeated attacks of erythema nodosum are extremely common in lepromatous leprosy. Attention was first drawn to it in 1912. Raised, tender nodules may cover the face, trunk, and extremities and be accompanied by malaise, arthralgia, neuritis, and fever. Occasionally, orchitis occurs. The occurrence of erythema nodosum in leprosy is not related to any form of therapy. It has been frequent and at times severe in those treated with dihydrostreptomycin or a thiourea as well as in the sulfone-treated patients. In mild cases no special treatment is usually necessary, and chemotherapy may be continued. When fever is high or other constitutional symptoms severe, specific treatment should be discontinued and bed rest instituted. Scores of remedies have been advocated, of which antipyretics, antihistamines, and potassium antimony tartrate are the most popular.[3] Whether these drugs are beneficial is doubtful. In acute and severe cases, cortisone or another corticosteroid may be used in the minimal dosage required to control the reaction and may be continued for about a week after the lesions begin to subside. In these patients, relief of the pain of acute neuritis is often dramatic. There is no evidence that leprosy is worsened by short courses of treatment with these hormones. In chronic, recurring erythema nodosum, however, much more experience is needed. Recurrences are not prevented, and whether they are lessened or worsened in severity is not known. At the National Leprosarium,[18] parenteral administration of cortisone or corticotropin (ACTH, Acthar, Corticotropin, Cortophin) has been continued as long as 10 months, in an attempt to control these reactions. In some patients, reactions persisted in spite of very high doses, but no serious complications had been observed to the time of report (1956). Controlled studies are necessary to evaluate the results of a long-term, low-dosage schedule as a supplement to sulfone treatment.

Progressive lepra reaction is much less frequent than erythema nodosum but much more severe. It is characterized by great extension of the cutaneous lesions, together with neuritis, high and long-continued fever, and cachexia. Since these progressive reactions threaten life, there may be no alternative to treatment with cortisone or corticotropin preparations. However, both physician and patient must recognize the probability that therapy may have to be continued for several months and must accept whatever untoward effects may ensue.

In the tuberculoid type of leprosy, the reactions are usually of shorter duration than in the lepromatous type and are thought by some leprologists to have a beneficial effect on the disease. They may, however, be alarmingly severe. The cutaneous lesions become reddened, and new ones appear. Myco. leprae is often readily demonstrable in smears from these lesions. As in the lepromatous type, neuritis, most frequently of the ulnar, is the most distressing feature. At times, it seems to be precipitated or worsened by sulfone therapy. Cortisone will control the pain temporarily, but further studies are required to determine whether it can lessen nerve damage and its sequelae.

Conclusions

The drugs of choice in the treatment of leprosy, taking both efficacy and cost into account, are those of the sulfone class. In suitable dosage, the parent sulfone, *p,p′*-sulfonyldianiline (DDS), gives the same results as any of the disubstituted compounds such as glucosulfone, sulfoxone, or solapsone. There are patients, however, who tolerate one of the latter better than DDS. There are also patients who do not respond satisfactorily to sulfone therapy. For these, dihydrostreptomycin or a diphenyl thiourea may be tried. In the lepromatous type, treatment should be continued indefinitely. In the tuberculoid type, there is a tendency toward spontaneous arrest, and, in many patients with only single macular lesions, specific therapy is not indicated. In active tuberculoid cases with multiple lesions, sulfones should be given, although evidence of their value is not conclusive.

The treatment of the reactions of leprosy constitutes the greatest difficulty, especially in the lepromatous type. It is true that in many such cases there is only erythema nodosum, with minor constitutional disturbance. This usually clears up without treatment. In other instances, the reaction is a progressive one, with severe constitutional symptoms and exacerbation of the leprotic lesions. The reaction may subside after weeks or months of illness. Sometimes it can be controlled with a corticosteroid compound. Certain cases baffle the skill of the physician, and death occurs from what is called "leprous cachexia," for lack of a better name.

The value of the sulfones in leprosy has been definitely established. Their effect, however, is bacteriostatic and not bactericidal. This conclusion follows from the slowness of clinical and bacteriological improvement and from the not infrequent occurrence of relapse after many months of treatment. Search for a more rapidly effective drug should be pressed with much greater vigor than is being done at present. The basic needs are a method of cultivation of the leprosy bacillus and an animal that is susceptible to the disease. Until at least one of these is found, the path of analogy is the most logical one to follow. Tuberculosis has been a valuable guide, but there are several other mycobacterial diseases which have been inadequately studied from the point of view of therapy. In addition, there are cultivable mycobacteria which have been very little used for screening. Every drug or antibiotic that shows significant action against any mycobacterium and is proved safe according to long-term toxicity studies should be tested in leprosy in humans.

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MEDICAL LICENSURE

THE Council on Medical Education and Hospitals presents its annual compilation on medical licensure in this issue of THE JOURNAL. The report includes statistics concerning the medical examination and licensure of physicians in the United States and its possessions for the year 1959, as well as comparative figures for previous years. Also included is information pertaining to the current regulations for medical licensure. The officers of the examining and licensing agencies have been most cooperative in the submission of the current data and information essential in the compilation of a report of this nature; for this assistance, the Council is deeply grateful.

The report further contains a review of the activities of the Federation of State Medical Boards of the United States and its plans for the future.

As a part of this annual study on licensure, the Council has included a section pertaining to the Educational Council for Foreign Medical Graduates and presents the results of the American Medical Qualifying Examination given in 1958 and 1959.

A section is included pertaining to boards of examiners in the basic sciences and the National Board of Medical Examiners.

Analysis of the statistical data and textual information reveals that, in 1959, a total of 15,954 licenses to practice medicine and surgery were issued by 54 boards authorized by law to grant licenses to practice the art and science of medicine. The 15,954 licenses issued last year represented 7,720 granted after a successful written examination and 8,234 granted by reciprocity and endorsement of state licenses or the certificate of the National Board of Medical Examiners. There was an increase of 714 in the total number of licenses issued in 1959, as compared with the previous year. The number of licenses issued by process of examination increased by 405 over the previous year; the number issued by reciprocity and endorsement of credentials was increased by 309.

Licentiates who received their first license to practice medicine and surgery during the calendar year of 1959 and who represent additions to the medical profession numbered 8,269. In this group, there were 1,626 foreign-trained physicians. In the same period, there were approximately 3,500 deaths of physicians reported to the offices of the American Medical Association. Thus, the physician population in the United States and its possessions was increased by about 4,800. Increases, as compared with similar figures for 1958, occurred in 29 states. There was no marked decrease evident in any state.

Last year, examination failures totaled 1,162. The total number of physicians examined was 8,996. Among the graduates from existing approved medical schools in the United States, only 3.5% failed in the written examinations. In Canada, 9% of the graduates of approved medical schools failed. Among graduates of unapproved medical schools at one time existing in the United States, 72.7% failed. The graduates of schools of osteopathy admitted to medical licensure examinations in several states had 16.5% failures, and 32.4% of the foreign-trained physicians examined for medical licensure last year failed. When the figures for these groups of examinees are combined, 12.9% of the total number of examinees failed in the written examinations.

The study includes other data on the licensing boards requiring an internship for licensure, regulations pertaining to the registration of interns and residents, licensure on the basis of government credentials, issuance of temporary and educational permits, limited and temporary licenses, the schedule of written examination dates and reciprocity meetings, citizenship requirements, medical license fees, and annual registration requirements.

The licensure of foreign-trained physicians is specifically referred to in the first section of the report and reveals that graduates of 244 foreign medical schools were examined for medical licensure in 1959 by 43 boards. Graduates of medical schools of the Philippines, Iceland, 18 South and Central American countries, 21 European countries, and 21 countries in Asia and Africa were represented at examinations. There were 2,766 foreign-trained physicians examined. Of these, 1,870 passed and 896 (32.4%) failed. More than 75 graduates from seven schools were examined, and 19 schools had 25 to 75 graduates examined for licensure in the United States in 1959. In a 14-year period, the report points out, there were 11,187 licenses issued after written examination to foreign-trained physicians and 2,322, by endorsement of credentials.

The second section of the Council's report pertains to the results of examinations and endorsement of credentials sponsored by 22 boards of examiners in the basic sciences. These boards have no licensing powers. A certificate of proficiency is issued that is a prerequisite to eligibility to practice. Such certificates were issued after written examination to 3,315 persons, and, by endorsement of credentials, 2,680 certificates were issued. The percentage of failures among examinees in the written examination for those boards reporting this information was 17.7. A candidate applying for a basic science certificate is not required by law to reveal his school of practice. The figures given, therefore, include graduates of all schools of the healing art.

The third section of the study deals with examinations given by the National Board of Medical Examiners. The examination of the National Board is given in three parts and may be taken during the course of education in medical school. The Board's certificate is accepted by the medical licensing authorities of the states, District of Columbia, and possessions, except in Arkansas, Florida, Georgia, Indiana, Louisiana, Michigan, and North Carolina. The purpose of the National Board is to administer an examination that may be accepted as an adequate qualification for a medical license. It is not a national licensing board. There were 3,377 licenses to practice medicine issued by endorsement of the certificate of the National Board by 43 state boards, the District of Columbia, Canal Zone, and Puerto Rico. The National Board also provides a service to medical schools using its examination for a variety of purposes. The most prevalent use of the examination in medical schools is for the purpose of a valid, comprehensive, and impartial evaluation of the student class at the end of the second and fourth years. There were 43 medical schools in which part 1, part 2, or both parts of the National Board examinations were taken by at least 75% of the students in the classes involved, during 1959.

The concluding section of the Council's report summarizes the results of the American Medical Qualification Examination administered by the Educational Council for Foreign Medical Graduates in 1958 and 1959. As of January 1, 1960, the Educational Council had examined 5,982 foreign medical graduates. Of these, 2,709 had been granted the standard certificate and 1,419 the temporary (two-year) certificate.

EXPIRED AIR RESUSCITATION DURING CARDIAC EMERGENCIES

All physicians have the responsibility to be prepared to carry out emergency measures for cardiac standstill or ventricular fibrillation. There is no time to send for help. If the patient is to survive, ventilation and circulation must be started in the first few minutes. Drastic measures may be indicated in the treatment of this drastic emergency.

If emergency thoracotomy is indicated, this procedure should be accompanied by restoration of pulmonary ventilation. While one physician opens the chest, another physician or trained aide must insure effective pulmonary ventilation. In the operating room and recovery ward, the anesthesiologist and his emergency equipment may be available and he should be summoned at once. Until he arrives, however, pulmonary ventilation can be adequately maintained without any equipment by the use of expired air, blowing one's own air into the nose or mouth of a victim.

Any artificial respiration, to be effective, depends on an open airway, and clearing the airway must be the first step. When the neck flexes and the jaw sags, the pharynx is obstructed. Backward tilting of the head at the atlanto-occipital joint opens the glottis and lifts the tongue from a blocking position in the pharynx. Further, if the jaw is moved cephalad simply by pressure against the chin, a patent airway is assured.

A wide, tight seal of the lips of the rescuer is made around the nose or mouth of the patient. The rescuer blows out until he sees the chest of the victim rise. This instruction applies whatever the size of the patient. It is possible to breathe rhythmically for a patient at the rate of 12 to 20 times per minute for long periods without fatigue or the necessity of relief. If the volumes inflated are two times the patient's basal tidal volumes, adequate oxygenation and carbon dioxide exchange are obtained.

Prompt restoration of good gas exchange is essential before a normal heart rhythm can be reestablished. We have had the happy experience of seeing a normal cardiac rhythm reappear while we were giving mouth-to-mask resuscitation in a patient with cardiac arrest (electrocardiographically confirmed). The circulation returned so quickly that emergency thoracotomy was avoided.

Among the advantages of expired air resuscitation are the large reserves of pressure and volume which may be used to overcome diminished pulmonary compliance of the victim. At times this therapy is more effective than oxygen administered by a mechanical resuscitator, which may have an inflation pressure inadequate for the circumstances in the patient with a "tight" chest.

Physicians and other hospital personnel may be called on to do mouth-to-nose or mouth-to-mouth resuscitation with no warning. The frequency of the emergency is greater in the hospital than in other areas. In the actual emergency the important points to be remembered are: 1. Clear the throat. 2. Tilt the head back, and 3. Blow.

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ECUMENICAL MEDICINE

Ecumenical (Gr., *oikoumenikos*—the inhabited world) medicine means different things to different physicians. It means a world-wide major program of medical missionary work to Dr. Paul S. Rhoads, Chairman of the Medical Committee of the Commission on Ecumenical Mission and Relations of the United Presbyterian Church in the United States.[1] One of the largest undertakings in this secular program is in Cameroun, a land south and west of Nigeria, in mid-Africa. There are 13 physicians assigned to Cameroun, working in 8 hospitals, 10 dispensaries, 4 leprosy projects, and one dental clinic.

Four projects are allocated to a single disease, leprosy. This will not be a surprise to the informed, however, since there are more than 12 million cases of leprosy in the world today. There are a total of 10 leprosy projects sponsored by the Presbyterian Ecumenical Program. In Pakistan the program supports five hospitals. There are three medical colleges in which the United Presbyterian Church participates, in cooperation with other Protestant churches of America and England—two are in India and one is in Korea. A total of 44 clinics or dispensaries and 27 nursing education programs in 15 countries are included—indeed a major undertaking.

Pertinent to the subject of medical missionaries is the resolution introduced by a member from Oregon which was passed subsequently by the House of Delegates at the Clinical Session in Dallas last autumn. The resolution recognized the lack of facilities for postgraduate medical education of members of the American medical profession who practice in foreign mission hospitals. The missions are far "removed from the usual opportunities for professional improvement, such as libraries, exhibits, lectures, conventions, medical motion pictures, and recordings for members of the medical staffs to keep alert of the advances of American medicine . . ." Hence it was "Resolved; That the House of Delegates of the American Medical Association does hereby recognize the responsibility of the Association for the postgraduate education of American physicians in the foreign missions field; and does hereby direct that an appropriate committee of the Association study and make recommendations regarding ways and means of bringing such educational facilities within the reach of these physicians."

Leprosy is one malady that need not be included in the postgraduate program. On the contrary, many of the medical missionaries can speak from practical experience of leprosy, a dread disease described in the Bible. It is not so dread a disease, however, as is implied by the outmoded term "leper." A visit to a leprosarium may be an enlightening clinical experience. In spite of the desirability of intelligent restriction of activity for patients with leprosy and the necessity for withdrawal from many phases of normal life, a leprosarium need not be a prison or a domicile of depression. The hospital remains the most desirable unit for the treatment of "open end" infective cases, so long as they are markedly so. Furthermore, isolation is necessary for the treatment of patients suffering from acute "reactional end" episodes of leprosy, for the surgical reconstruction of patients with mutilations, and for the training of personnel and other administrative purposes, including the management of recalcitrant patients.

In the search for a cure for leprosy, two serious obstacles are presented. There is no reliable method of cultivation of Mycobacterium leprae, nor is there an experimental animal susceptible to this organism. Drugs useful in the control of the disease most similar to leprosy, i. e., tuberculosis, are helpful but not specific. The parent sulfone, p,p′-sulfonyldianiline (DDS), is probably the drug of choice. Dihydrostreptomycin or diphenyl thiourea may be used if the patient fails to respond to one of the sulfones. The sulfones are bacteriostatic, not bactericidal. They act by depriving the bacillus of one of the essential amino acids (p-aminobenzoic acid). Treatment must be continued as long as the disease is active. This is but one of the many clinical problems that the medical missionary encounters in his day-by-day practice of ecumenical medicine.

NEOLOGOPOIESIS

The invention of a new word is not a unique phenomenon in medicine. Several hundred units of speech are added to our literature each year. If one is addicted to neologopoiesis, autologous in this editorial, two books may be read with profit. The third edition of Ffrangcon Roberts' "Medical Terms"[1] has just been published. Perry Pepper's "Medical Etymology"[2] appeared several years ago. According to Roberts, "The rapid accumulation of medical knowledge and the changes in medical conceptions make the invention of new words inevitable. Some physicians, however, believe that this process is taking place more rapidly than is justified; they deplore the excessive use of jargon. Some go as far as to complain that many words which they read are not to be found in the dictionaries, but words are not born in dictionaries; they are born in men's minds."

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[1] The other physician members of this committee include William J. Barnes, M.D., Great Barrington, Mass.; Morris A. Bowie, M.D., Bryn Mawr, Pa.; Horace Giffen, M.D., Omaha, Neb.; Alonzo Peeke, M.D., Volga, S. D.; Edgar L. Ralston, M.D., Philadelphia; Frederick G. Scovel, M.D., New York; and John Waugh, M.D., Rochester, Minn. Theodore Stevenson, M.D., New York, a former missionary doctor, is full-time secretary.

The coinage of a new word that becomes accepted in currency of the realm may be a praiseworthy pursuit. If existing words are inadequate to convey the impression desired, it may be concluded that progress is being made. The semantic ideal implies one word for each meaning and one meaning for each word. The organic chemist has been forced to invent new words to identify each of the multitude of new compounds that are discovered at an increasingly fabulous rate. A perusal of Merck's Index reveals the validity of this statement. Another maker of new words is the person assigned to the brand-name division of a pharmaceutical firm. His position at the moment is somewhat insecure, but he will probably survive in spite of the arguments in favor of exclusive use of generic terms.

Greek and Latin are the basis of the majority of medical terms. It is regrettable that many young physicians have studied neither of these classical languages in liberal arts college. It would be much easier to understand a number of medical terms and many would be more easily retained in the cortical background if some knowledge of at least Latin were incorporated in the scholastic armamentarium. Not only is a knowledge of the classics helpful in understanding medical terms, the story behind the derivation of many words is an interesting exercise. A few examples will illustrate the metamorphosis.

Astragalus comes directly from the Greek, *astragalos,* a set of dice. The Greeks of pre-Hellenic times carved dice from the second vertebrae, the astragalos, of sheep. Several centuries later the heel bone of the horse was used for the same purpose. In human osteology, astragalus is one of the bones of the feet, some distance removed from the crap table. *Meconium* is from the Greek, *mekonion,* poppy juice; the root is *mekon,* poppy. Poppy juice is a viscous, greenish substance similar to the first feces of the newborn infant. Furthermore, meconism is a synonym in current use for opium addiction. *Pituitary* is derived from mucus. The Greek, *pituita,* referred to the mucus secretion from the nose and mouth. Nasal secretions at the time of Galen were believed to originate in the brain and to pass through the cribriform plate of the ethmoid bone. And, finally, *muscle* is from the Latin, *musculus,* mus, a mouse, and the diminutive suffix, ulus. Thus a muscle was a mouse running subcutaneously.

During the thousand years when European medicine and science were influenced by the Moslem empire, the classical Greek and Latin medical treatises were the basis of the practice of medicine. Many Arabic words were incorporated in the writings of the Dark Ages. The result was a mixture of Greek, Latin, and Arabic. The impact was probably felt more in mathematics than in medicine, for the word *algebra* is of Arabic derivation, and the supplanting of the unwieldy Greek and Latin number-systems with the Arabic numerals we use today was one of the great advances that was made in arithmetic. With the beginning of the Renaissance, the humanist turned back to the Greek and Latin texts because of the great difficulty experienced in translating Arabic. Hence, few Arabian stems or words are in current medical literature. The use of *mater* in the sense of *membrane* is a medieval translation into Latin of the Arabic for mother. *Dura mater* is the hard mother that protects the brain; *pia mater* is the tender mother. Nucha comes directly from the Arabic, neck. There are a few German words in good standing in English medicine. The best known is *anlage* (primordium), used in embryology.

There are a few modern medical words that are bizarre and carry a false meaning when translated literally. Roberts notes that *hemophilia* means loving of blood, *lithotomy* should be *lithectomy* since it is intended to "cut out the stone," and *thalassemia* means "sea in the blood"; *thalassanemia* is the correct term.

If one feels the urge to make a new word, it is best to learn the technique in order to avoid making a bad one. It is hoped that *neologopoiesis* is not in this category. By all means do not indulge in *coprolalia.*

THE PRINCIPLES OF DERIVATION

Innumerable names are derived from resemblance to buildings, animals and plants or their parts, to musical instruments, articles of adornment, agricultural implements, tools and weapons. . . .

In order to illustrate the derivation of names from surrounding objects we may reflect upon domestic life in Graeco-Roman times. An open space for assembly or marketing was called *agora* (hence *agoraphobia,* fear of open spaces). An enclosed space, if large, was called *claustrum* (*claustrophobia,* fear of being shut in), and, if small, *areola,* (*areolar* tissue, i. e. tissue of small spaces). In a house the *vestibulum* led into the *atrium* (to us synonymous with *auricle*). This may have been so-called because it had a fire in the middle of the room and therefore had blackened walls (*ater,* black). An inner room or bedroom in Greece was called *thalamos,* a term applied by Galen to the inner chambers of the brain.—Roberts, F., Medical Terms: Their Origin and Construction, Springfield, Ill., Charles C Thomas, Publisher, 1959, p. 26.

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1. Roberts, F.: Medical Terms, Their Origin and Construction, ed. 3, Springfield, Ill., Charles C Thomas, Publisher, 1959.
2. Perry Pepper, O. H.: Medical Etymology, Philadelphia, W. B. Saunders Company, 1949.

THE PRESIDENT'S PAGE

A MONTHLY MESSAGE

Evidence continues to mount that a plan to provide hospital and medical care for the elderly must be kept out of federal government control, out of the Social Security system, and out of the political arena.

I am gratified to see so many newspaper editorials agree on these basic issues. I also am happy to read that so many are emphasizing that no program should drive either private insurance companies or nonprofit organizations like Blue Cross–Blue Shield out of business . . . that the private and sensitive relationship of patient and physician must not be destroyed . . . that all compulsory aspects must be omitted . . . and that no program should be inflationary, for it is essential to maintain the purchasing power of fixed pension and annuity benefits.

Furthermore, I strongly support the following ideas as presented recently by some leading newspapers and by many medical spokesmen:

1. President Eisenhower should call a conference of House and Senate leaders from both political parties to discuss the subject of how best to provide hospital and medical insurance for the elderly. These leaders should include Senate Majority Leader Lyndon Johnson (D., Tex.), Senate Minority Leader Everett Dirksen (R., Ill.), House Speaker Sam Rayburn (D., Tex.), House Minority Leader Charles Halleck (R., Ind.), and Rep. Wilbur D. Mills (D., Ark.), Chairman of the House Ways and Means Committee.

This group would take the issue out of politics in an election year. It would seek to find what is best for the older people, and what is best for the country as a whole.

2. An alternate suggestion, and an excellent one, is that there is no crisis at the moment, and that it would be wise for Congress to wait until the White House Conference on Aging in January, 1961. There is no doubt that the issue of the elderly is important and complex; that is why the conference on aging was ordered originally and why commissions in every state have been gathering data on the problems of the aged.

I think that Congress should resist pressure from those groups insisting on hasty political and almost irreversible legislation now. There is no alarming crisis and there is no pressing need to take drastic action. Indeed, a vote-getting measure now could do more long-range harm than good. Already the needy aged are receiving health care through Old Age Assistance programs. Millions are receiving pensions and annuities. Religious groups are expanding their aid and care to the aged. Doctors of medicine are guaranteeing medical care to the near-needy aged. Most important of all, most older persons are living healthily, happily, and usefully.

Whether the President calls a Democratic-Republican summit conference on the subject or whether Congress itself decides to wait for the complete story on the aged in January, I believe it is imperative that the political aspects of the issue be eliminated. If either course is followed, leaders of both parties should exert their influence to prevent election-minded legislators from pushing through any plan designed either wholly or partly to garner votes this year.

I believe that a sensible, economical health care program for the aged—with freedom preserved and security promoted—can be limited to support for the needy and the near-needy aged. For those outside these categories the mechanism of voluntary health insurance can and should be used to provide and to improve health care.

Louis M. Orr, M.D.
Orlando, Fla.

STATE BOARD NUMBER, COUNCIL ON MEDICAL EDUCATION AND HOSPITALS

FIFTY-EIGHTH ANNUAL PRESENTATION OF LICENSURE STATISTICS BY THE COUNCIL ON MEDICAL EDUCATION AND HOSPITALS OF THE AMERICAN MEDICAL ASSOCIATION

The data in the following annual report on Medical Licensure Statistics have been compiled by the staff under the supervision of Mrs. Anne Tipner, Assistant to the Secretary of the Council on Medical Education and Hospitals.

WALTER S. WIGGINS, M.D., *Secretary*
Council on Medical Education and Hospitals

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ACKNOWLEDGMENT

This report is the 58th annual compilation of information and statistics pertaining to medical licensure in the United States and its possessions. As in previous years, data are included pertaining to boards of examiners in the basic sciences and the National Board of Medical Examiners. There is also presented a summary account of the activities of the Federation of State Medical Boards of the United States and the Educational Council for Foreign Medical Graduates.

The Council on Medical Education and Hospitals desires to express appreciation on behalf of the American Medical Association to those individuals and organizations who have cooperated in furnishing the information on which this current report is based.

ACTIVITIES OF THE FEDERATION OF STATE MEDICAL BOARDS OF THE UNITED STATES

The following material reviewing the activities of the Federation of State Medical Boards of the United States has been submitted by the Associate Secretary of the Federation.

The Federation continued its studies in 1959 in the field of comparative values involved in evaluating the backgrounds of physicians from all parts of the world. The annual program for the February, 1960, meeting at the Annual Congress on Medical Education and Licensure was designed to acquaint examiners with the problems in medical education in other countries, particularly those countries where the Rockefeller Foundation has an interest in promoting improvement in medical schools.

For many years to come, the Federation will have a number of interesting challenges dealing with the diversified levels of medical education the state boards will encounter in the records of applicants for licensure. The Federation has, as no other organization in the health field, the obligation to understand the nature and quality of international medical education. It has the onus, too, to foresee and prepare for the more definitive needs of a large segment of the house staffs of American hospitals. It must constantly reevaluate its attitude and position in respect to results already evident from the two world conferences on medical education.

In reviewing its status at the end of a decade, the Federation could survey a wide range of progress, from the indecision anxiety about the foreign graduate problem in 1950, to the far better understanding and satisfaction it had in culminating its initial studies in this field with a study of compara-

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In the descriptive data, reference is made to the total number of boards for which figures are reported. The figures include the examining and licensing boards in the United States, the Canal Zone, Guam, Puerto Rico, and the Virgin Islands. Alaska and Hawaii are listed among other states in this study.

tive values in medical education at the international level. There was evidence, also, that the process of educating and training examiners in the identification of fitness had been far more successful than anticipated. The Federation had, in one busy decade, created a greater interest in its own potential than ever before. It had, in fact, moved from a state, to a national, to an international level of thinking about its central objective of fitness evaluation.

It is now clear that the concept of fitness involves some thinking about fitness as a continuing factor, much as the modern concept of education is one of a life-long effort. In the coming year, the Federation will move in the direction of a resurveying of the field of discipline. Representatives of the Federation have cooperated with the Medical Disciplinary Committee of the American Medical Association in its regional meetings. The goal will be that of uniform interstate action and procedure in handling the problem of discipline in the profession.

The Federation watched, with great interest, the wide and rapid acceptance of the Educational Council for Foreign Medical Graduates. The Federation will continue to observe the assistance this organization renders to many state boards. The Federation anticipates that the effect on levels of medical education in many parts of the world will become increasingly noticeable. Being a major partner in the enterprise of the Educational Council for Foreign Medical Graduates, the Federation came into a deeper appreciation of the interest and contributions made by the other major partners, particularly the American Medical Association.

Finally, the Federation considers that it made a significant contribution to the program of the 1960 Annual Congress on Medical Education and Licensure, with the contributions of Dr. John Weir of the Rockefeller Foundation and the panel of foreign scholars.

EDUCATIONAL COUNCIL FOR FOREIGN MEDICAL GRADUATES

The Educational Council for Foreign Medical Graduates began operation on Oct. 1, 1957. Sponsoring agencies are the American Hospital Association, the American Medical Association, the Association of American Medical Colleges, and the Federation of State Medical Boards of the United States. The Board of Trustees of the Educational Council includes representatives from each of these organizations and two members representing the public at large. Its stated purpose is to provide information to foreign medical graduates, to translate and evaluate foreign educational credentials, and to test the foreign medical graduate's command of English and his basic knowledge of medicine. Later, in this study, there is a section pertaining to the results of the American Medical Qualification Examinations given in 1958 and 1959.

MEDICAL LICENSURE STATISTICS

The tables referring to medical licensure include figures for the number of candidates examined for medical licensure, in 1959, and, also, for those licensed on the basis of reciprocity or endorsement of credentials. Other data pertain to the regulations for medical licensure of physicians who secured their professional training in the United States and Canada and those educated in other countries. The state boards are discussed first, followed by the basic science board, the National Board of Medical Examiners, and the Educational Council for Foreign Medical Graduates.

STATE BOARDS OF MEDICAL EXAMINERS

Licenses Issued

During 1959, there were 15,954 licenses to practice medicine issued by 54 legally constituted medical examining boards granted authority to issue licenses to practice medicine and surgery. The number licensed by each board on the basis of written examination or by endorsement of credentials is shown in table 1. Of the 15,954 licenses issued, 7,720 were granted after written examination and 8,234 by reciprocity or endorsement of state licenses or the certificate of the National Board of Medical Examiners.

It does not follow that all physicians licensed after written examination were tested in a given year. Thirty-eight licensing boards require a year of internship as a prerequisite for licensure. A number of the boards permit the candidate for medical licensure to take the written examination after completion of the internship, and, if it is successful, the license is issued and dated on completion of the internship requirement. Licenses are also withheld in some states for other technicalities. As a rule, the licenses of those examined in December are dated and issued in the following year. The figures in table 1, therefore, will not correspond with those in succeeding tables which deal entirely with physicians examined for licensure in 1959, but they do include persons who may have been licensed in more than one state in a given year. In tables 11, 12, and 13, presented later in this report, the number of physicians who secured their first licenses to practice medicine in 1959 and who thus represent additions to the medical profession in the United States and its possessions can be noted.

The greatest number of licenses issued in 1959, both by examination and by reciprocity and endorsement of credentials, was granted by California. This state issued 2,277 licenses; New York issued 1,648; Ohio, 855; Pennsylvania, 785; and Illinois, 745. More than 500 physicians were registered in Michigan, New Jersey, and Texas. The fewest (21) were licensed in Wyoming, whereas Alaska, Delaware, Idaho, Montana, Nevada, New

Hampshire, North Dakota, South Dakota, and Vermont each issued less than 50 licenses. In 1959, the Canal Zone licensed 1 physician; Puerto Rico, 153; and the Virgin Islands, 5. No physicians were licensed for civilian practice in Guam during the year.

TABLE 1.—*Licenses Issued, 1959*

	Examination	On Basis of Reciprocity and Endorsement	Total
Alabama	134	72	206
Alaska	3	19	22
Arizona	24	121	145
Arkansas	73	29	102
California	545	1,732	2,277
Canal Zone	...	1	1
Colorado	56	126	182
Connecticut	162	239	401
Delaware	16	15	31
District of Columbia	11	167	178
Florida	350	...	350
Georgia	270	91	361
Hawaii	28	26	54
Idaho	8	40	48
Illinois	526	219	745
Indiana	176	197	373
Iowa	116	85	201
Kansas	64	63	127
Kentucky	101	90	191
Louisiana	261	114	375
Maine	26	44	70
Maryland	256	157	413
Massachusetts	56	400	456
Michigan	331	189	520
Minnesota	193	177	370
Mississippi	112	31	143
Missouri	296	121	417
Montana	3	46	49
Nebraska	121	20	141
Nevada	...	32	32
New Hampshire	5	36	41
New Jersey	193	386	579
New Mexico	3	71	74
New York	479	1,169	1,648
North Carolina	211	75	286
North Dakota	14	16	30
Ohio	495	360	855
Oklahoma	87	49	136
Oregon	33	96	129
Pennsylvania	529	256	785
Puerto Rico	124	29	153
Rhode Island	30	32	62
South Carolina	94	42	136
South Dakota	12	27	39
Tennessee	201	100	301
Texas	344	245	589
Utah	27	71	98
Vermont	29	14	43
Virginia	275	128	403
Virgin Islands	5	...	5
Washington	62	163	225
West Virginia	27	77	104
Wisconsin	119	112	231
Wyoming	4	17	21
Totals	7,720	8,234	15,954

There was an increase of 714 in the total number of licenses issued in 1959, as compared with the previous year.[1] The number of licenses issued after examination increased by 405 over the previous year, and the number issued by reciprocity and endorsement of credentials was increased by 309.

Totals of the physicians licensed in 24 previous years and for 1959, both by examination and reciprocity or endorsement of credentials, are included in table 2. The variations shown for the years from 1936 to 1941, inclusive, were due to the increase in the licensure of foreign-trained physicians. The increases in succeeding years reflect the increase in the production of physicians, the mobility of physicians, as well as the licensure of foreign-trained physicians. In 25 years (1935-1959), the number of medical licenses issued in the United States and its possessions totaled 298,440; 161,297 of which were issued after written examination and 137,143, by endorsement of credentials.

Candidates Examined by Medical Examining Boards

Compilations referred to those examined for medical licensure in 1959 by 54 licensing boards are given in table 3. The data are presented for 50 states, the District of Columbia, Puerto Rico, the Canal Zone, the Virgin Islands. For each board is recorded the number who passed and failed, the medical school of graduation, the percentage of failures for each school and for each licensing board, the number of states in which graduates of a given school were examined, and the percentage of failures for each school and each state. Medical schools that are no longer in operation in the United States, foreign faculties of medicine, and schools of osteopathy are not listed by name, but the numbers examined in each state in these four categories are included after those for existing medical schools in the United States and Canada.

TABLE 2.—*Licenses Issued, 1935-1959*

Year	Examination	Reciprocity and Endorsement	Total
1935	5,725	2,194	7,919
1936	6,276	2,773	9,049
1937	6,629	3,205	9,834
1938	6,557	2,956	9,513
1939	6,400	2,872	9,272
1940	6,289	2,866	9,155
1941	6,057	2,762	8,819
1942	6,152	2,469	8,621
1943	6,062	2,340	8,402
1944	7,080	2,596	9,676
1945	5,580	3,622	9,202
1946	6,567	9,669	16,236
1947	6,763	7,701	14,464
1948	5,997	7,595	13,592
1949	5,252	6,929	12,181
1950	5,454	6,755	12,209
1951	5,713	6,225	11,938
1952	6,212	7,016	13,228
1953	6,565	7,869	14,434
1954	6,827	8,202	15,029
1955	7,379	7,461	14,840
1956	7,122	7,421	14,543
1957	7,604	7,486	15,090
1958	7,315	7,925	15,240
1959	7,720	8,234	15,954
Totals	161,297	137,143	298,440

TABLE 3.—Candidates Ex

Marginal Number	School	1 Alabama		2 Alaska		3 Arizona		4 Arkansas		5 California		6 Colorado		7 Connecticut		8 Delaware		9 District of Columbia		10 Florida		11 Georgia		12 Hawaii		13 Idaho		14 Illinois		15 Indiana		16 Iowa		17 Kansas		18 Kentucky		19 Louisiana		20 Maine		21 Maryland		22 Massachusetts
		P	F	P	F	P	F	P	F	P	F	P	F	P	F	P	F	P	F	P	F	P	F	P	F	P	F	P	F	P	F	P	F	P	F	P	F	P	F	P	F	P	F	P
	ALABAMA																																											
1	Medical College of Alabama, Birmingham	61	0																	7	2																							
	ARKANSAS																																											
2	Univ. of Arkansas School of Med., Little Rock							68	2											2	0																	2	0					
	CALIFORNIA																																											
3	Coll. of Med. Evangelists, Loma Linda, Los A.									43	4									4	2	4	0			1	0															3	0	
4	Univ. of California School of Med., Los Angeles									42	0	2	0																															
5	Univ. of So. California School of Med., Los A.									63	0									2	0							1	1									1	0					
6	Stanford Univ. School of Med., Palo Alto									39	2									1	0	1	0																					
7	Univ. of Calif. School of Med., San Francisco					2	0			78	0									1	0																							
	COLORADO																																											
8	University of Colorado School of Med., Denver					4	0			3	0	72	0							2	0	1	0	0	1			1	0					1	0									
	CONNECTICUT																																											
9	Yale University School of Medicine, New Haven																			3	2																							
	DISTRICT OF COLUMBIA																																											
10	Georgetown Univ. School of Med., Washington									1	0			1	1					9	4																					1	0	0
11	George Wash. Univ. School of Med., Washington							1	0					2	0			2	0	5	2																	1	0			1	0	
12	Howard Univ. College of Med., Washington									3	1									1	0	3	0					3	1													42	10	
	FLORIDA																																											
13	Univ. of Miami School of Med., Coral Gables									1	0									57	1	9	0															1	0					
	GEORGIA																																											
14	Emory Univ. School of Med., Emory University																			46	1	65	0																					
15	Medical College of Georgia, Augusta																			12	2	88	0																					
	ILLINOIS																																											
16	Chicago Medical School																			7	1	1	0	1	0			1	0									1	0					
17	Northwestern Univ. Medical School, Chicago			1	0	1	0			17	0							0	1	11	1			1	1			24	0	4	0					1	0	4	0					1
18	Stritch Schl. of Med., of Loyola Univ., Chicago																			3	11							32	1			1	0					2	0					1
19	University of Chicago, The School of Medicine									2	0			1	0					2	0	2	0					8	0									1	0			1	0	
20	University of Illinois College of Med., Chicago							1	0	3	0	1	0							5	1							55	1	1	0							1	0					0
	INDIANA																																											
21	Indiana University School of Med., Indianapolis																			21	4							6	0	13	10													
	IOWA																																											
22	State Univ. of Iowa Coll. of Med., Iowa City									0	1									0	1							2	0	1	0	97	0									1	0	
	KANSAS																																											
23	University of Kansas School of Medicine, Lawrence, Kansas City											1	0							2	0							1	0			1	0	23	0			1	0					
	KENTUCKY																																											
24	University of Louisville School of Medicine																			8	3							3	0							82	0							
	LOUISIANA																																											
25	Louisiana State University School of Medicine New Orleans									1	0									9	0																	110	0					
26	Tulane Univ. School of Med., New Orleans					1	0			2	0									25	0			1	0			1	2									113	1					
	MARYLAND																																											
27	Johns Hopkins Univ. School of Med., Baltimore									1	0					2	0			5	0							2	1													46	2	
28	University of Maryland School of Medicine and College of Physicians and Surgeons, Baltimore											1	0							8	1			2	0			1	0													68	1	
	MASSACHUSETTS																																											
29	Boston University School of Medicine																			3	0									1	0													1
30	Harvard Medical School, Boston	1	0							2	0									8	1	2	0							3	0							2	0					0
31	Tufts University School of Medicine, Boston																			2	0																	1	0					0
	MICHIGAN																																											
32	University of Michigan Med. School, Ann Arbor									3	0			1	0	1	0			5	4			2	0			4	0									1	0					1
33	Wayne State Univ. College of Med., Detroit																			2	1																							
	MINNESOTA																																											
34	Univ. of Minnesota Med. School, Minneapolis									1	0									3	0			11	0																			
	MISSISSIPPI																																											
35	Univ. of Mississippi School of Med., Jackson																			1	0							1	0															
	MISSOURI																																											
36	University of Missouri School of Med., Columbia																			0	1			1	0													1	1			1	0	
37	Saint Louis University School of Medicine							1	0											8	3							0	2															
38	Washington Univ. School of Med., St. Louis																			7	1			2	0			4	0															
	NEBRASKA																																											
39	Creighton Univ. School of Medicine, Omaha					2	0			5	1			0	1					2	1			1	0					1	0	1	0	1	0									
40	Univ. of Nebraska College of Medicine, Omaha																			6	0	2	0					3	0			1	0											
	NEW YORK																																											
41	Albany Medical College of Union University																			2	1									2	0													
42	University of Buffalo School of Medicine																			6	2									1	0													
43	Albert Einstein College of Medicine of Yeshiva University, New York City																																											
44	Columbia University College of Physicians and Surgeons, New York City					1	0													12	1	1	0			1	0	1	0									2	0					
45	Cornell Univ. Medical College, New York City							1	0			1	0							4	1	1	0			1	0							1	0			1	1	1	0			
46	New York Medical College, Flower and Fifth Avenue Hospitals, New York City																			12	1	1	0																					
47	New York Univ. College of Med., New York City													1	0					10	4																							
48	State University of New York, Downstate Medical Center, New York City																			9	1									1	0							1	0					
Marginal Number		1		2		3		4		5		6		7		8		9		10		11		12		13		14		15		16		17		18		19		20		21		22

P—Passed; F—Failed

F	27 Montana P F	28 Nebraska P F	29 Nevada P F	30 New Hampshire P F	31 New Jersey P F	32 New Mexico P F	33 New York P F	34 North Carolina P F	35 North Dakota P F	36 Ohio P F	37 Oklahoma P F	38 Oregon P F	39 Pennsylvania P F	40 Rhode Island P F	41 South Carolina P F	42 South Dakota P F	43 Tennessee P F	44 Texas P F	45 Utah P F	46 Vermont P F	47 Virginia P F	48 Washington P F	49 West Virginia P F	50 Wisconsin P F	51 Wyoming P F	52 Puerto Rico, Canal Zone, and Virgin Islands P F	53 Totals	54 Examined—Passed	55 Examined—Failed	56 % Failed	57 No of Boards Examined by	Marginal Number
																											71	69	2	2.8	3	1
							2 1																				77	74	3	3.9	4	2
													2 0		1 0											1 0	66	60	6	9.1	9	3
																											44	44	0	0.0	2	4
																											68	67	1	1.5	4	5
																				1 0							45	43	2	4.4	5	6
																											81	81	0	0.0	3	7
																1 0		1 0							3 0		91	90	1	1.1	12	8
													1 0														6	4	2	33.3	2	9
					2 0		2 1						7 0	1 0				1 0		1 0			1 0				35	27	8	22.9	12	10
							1 0						1 0				1 0	2 2									21	17	4	19.0	10	11
					2 0		4 4	2 0					1 0								7 1					1 0	87	70	17	19.5	12	12
																											69	68	1	1.4	4	13
							2 1																				115	113	2	1.7	3	14
																											102	100	2	2.0	2	15
															1 0												13	12	1	7.7	6	16
0					2 0					5 0		1 0					1 0	4 0	1 0			2 1	1 0	6 0			107	103	4	3.7	23	17
					1 0					9 0			1 0														64	59	5	7.8	10	18
0					1 0		3 1						1 0											1 0			27	26	1	3.7	13	19
0							2 0	1 0		2 0		2 0					1 0	3 7						3 0			90	86	4	4.4	18	20
																				1 0							169	165	4	2.4	4	21
0																		2 0									109	107	2	1.8	11	22
0							3 1					1 0															52	51	1	1.9	9	23
									1 0				1 0														100	97	3	3.0	7	24
																											120	120	0	0.0	3	25
							1 1								1 0												153	149	4	2.6	9	26
				1 0			1 0	1 0					1 0							1 0	1 0						67	64	3	4.5	12	27
													1 0					1 0	1 0							1 0	88	85	3	3.4	10	28
													1 0														7	6	1	14.3	4	29
					1 0		1 0	3 0		1 0				2 0				4 0		2 0							35	33	2	5.7	15	30
													3 0														7	6	1	14.3	4	31
1 0							1 1			4 0		1 0							1 0								206	201	5	2.4	15	32
																											68	67	1	1.5	2	33
																			1 0								122	122	0	0.0	5	34
																											63	63	0	0.0	3	35
2 0																											35	34	1	2.9	4	36
0							2 1						1 0				1 0	1 0									134	128	6	4.5	11	37
0							1 0										1 0			1 0		1 0					98	97	1	1.0	8	38
	1 0	53 1			1 0		1 0			1 0			1 0			1 0											80	76	4	5.0	17	39
		67 0																				1 0					80	80	0	0.0	6	40
																		2 0		1 0							8	7	1	12.5	4	41
							1 0																				11	9	2	18.2	4	42
																											..	..	..	..	..	..
					2 0		4 1	3 0		1 0			1 0				1 0	1 0								1 0	36	34	2	5.6	16	44
				1 0				2 0		1 0			1 0				1 0	1 0		1 0							22	20	2	9.1	16	45
							3 2						1 0														20	17	3	15.0	4	46
					1 0											1 0											17	13	4	23.5	4	47
							2 0	1 0						1 0						1 0			1 0				19	18	1	5.3	9	48

Marginal Number	School	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23
		Alabama	Alaska	Arizona	Arkansas	California	Colorado	Connecticut	Delaware	District of Columbia	Florida	Georgia	Hawaii	Idaho	Illinois	Indiana	Iowa	Kansas	Kentucky	Louisiana	Maine	Maryland	Massachusetts	Michigan
		P F	P F	P F	P F	P F	P F	P F	P F	P F	P F	P F	P F	P F	P F	P F	P F	P F	P F	P F	P F	P F	P F	P F
	NEW YORK—continued																							
49	Univ. of Rochester School of Med. and Dentistry						1 0				3 0													
50	State University of New York, Upstate Medical Center, Syracuse										2 1													
	NORTH CAROLINA																							
51	University of North Carolina School of Medicine, Chapel Hill										4 0									0 1				
52	Duke University School of Medicine, Durham										22 1	1 0												
53	Bowman Gray School of Medicine of Wake Forest College, Winston-Salem					1 0					7 2		1 0		1 0									1 0
	OHIO																							
54	University of Cincinnati College of Medicine										6 2				3 0				1 0					
55	Western Reserve Univ. School of Med., Cleveland		1 0								2 2			1 0										
56	Ohio State Univ. College of Med., Columbus					1 0					10 1		1 0		1 0									
	OKLAHOMA																							
57	University of Oklahoma School of Medicine, Oklahoma City						1 0				2 2				1 0					2 0				1 0
	OREGON																							
58	University of Oregon Medical School, Portland					7 0				1 0	3 0		1 0	2 0	2 0					1 0		2 0		1 0
	PENNSYLVANIA																							
59	Hahnemann Medical College and Hospital of Philadelphia					3 0			2 0	1 0	7 4												1 0	1 0
60	Jefferson Medical College of Philadelphia					3 0			2 0		15 4					1 0				2 0			1 0	1 0
61	Temple Univ. School of Med., Philadelphia					7 0		1 0	3 0		6 0	2 0			0 1	1 0			1 0					1 0
62	Univ. of Pennsylvania Sch. of Med., Philadelphia					5 0	1 0	2 0	3 0		7 1		1 0							1 0	1 0	3 1	1 1	
63	Woman's Medical College of Pennsylvania, Philadelphia			1 0		4 0					1 0	1 0	1 0		1 0								1 0	
64	University of Pittsburgh School of Medicine			1 0		7 0					5 3												1 0	
	PUERTO RICO																							
65	Univ. of Puerto Rico School of Med., San Juan																							
	SOUTH CAROLINA																							
66	Medical College of South Carolina, Charleston										4 0													
	TENNESSEE																							
67	Univ. of Tennessee College of Med., Memphis	1 0	1 0	2 0		1 0					21 2				3 0									
68	Meharry Medical College, Nashville					1 0						63 0									1 0			2 0
69	Vanderbilt University School of Med., Nashville										7 0	1 0	0 1		1 0					1 0				
	TEXAS																							
70	University of Texas Southwestern Medical School, Dallas										2 0													
71	University of Texas Med. Branch, Galveston				1 0						2 0		1 0							1 0				
72	Baylor University College of Medicine, Houston														1 0					1 0				
	UTAH																							
73	Univ. of Utah School of Med., Salt Lake City			1 0		10 0																	2 1	
	VERMONT																							
74	Univ. of Vermont College of Med., Burlington										2 1													
	VIRGINIA																							
75	Univ. of Virginia School of Med., Charlottesville										8 0	1 0												
76	Medical College of Virginia, Richmond					1 0					12 0	1 0								2 0				
	WASHINGTON																							
	Univ. of Washington School of Med., Seattle			1 0		5 0	1 0				1 0			1 0	3 0									
	WISCONSIN																							
	iv. of Wisconsin Medical School, Madison					6 0	3 0	1 0			3 1					2 0				1 0				1 0
	arquette Univ. School of Medicine, Milwaukee	1 0				11 0					2 0		1 0		9 0					2 0				1 1
	CANADA																							
	niv. of Alberta Faculty of Med., Edmonton					6 0										2 0								
	niversity of British Columbia School of Medicine, Vancouver					6 0	1 0																	
2	Univ. of Manitoba Faculty of Med., Winnipeg					7 0								1 0	1 0	2 0			1 0					1 0
83	Dalhousie Univ. Faculty of Med., Halifax	1 0																			3 1		0 1	2 0
84	Queen's Univ. Faculty of Medicine, Kingston					2 1				1 0												1 0		1 0
85	University of Western Ontario Faculty of Medicine, London			0 1		2 0				1 0														3 0
86	University of Ottawa Faculty of Med., Ottawa					4 0					2 0				1 0									3 0
87	University of Toronto Faculty of Medicine, Toronto					5 0					0 1					1 0						2 0		2 1
88	McGill University Faculty of Medicine, Montreal					7 0			1 0						1 0								3 0	2 0
89	University of Montreal Faculty of Medicine, Montreal					1 1																	0 1	
90	Laval University Faculty of Medicine, Quebec					3 2															1 0		0 1	1 0
91	University of Saskatchewan College of Medicine, Saskatoon					1 0																		
	OTHERS																							
92	Foreign Medical Faculties			7 2		85 54	2 0	136 76	1 1	14 0	32 10	19 2	9 3		345 229	15 2	1 0	9 0			19 5	51 12	42 32	33 1
93	Unapproved Medical Schools										1 0				0 1								0 13	
94	Schools of Osteopathy						3 1	0 1	1 1						8 2			2 0					0 1	
95	Totals	65	3	27	75	579	92	225	18	21	654	272	34	8	778	178	102	37	86	264	32	250	113	33
96	Totals Examined—Passed	65	3	24	73	512	91	146	16	20	561	270	28	8	536	176	102	37	86	261	26	223	56	32
97	Totals Examined—Failed	0	0	3	2	67	1	79	2	1	93	2	6	0	242	2	0	0	0	3	6	27	57	1
98	Percentage Failed	0.0	0.0	11.1	2.7	11.6	1.1	35.0	11.1	4.8	14.2	0.7	17.6	0.0	31.1	1.1	0.0	0.0	0.0	1.1	18.7	10.7	50.4	3.0
	Marginal Number	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23

P—Passed; F—Failed

27 Montana		28 Nebraska		29 Nevada		30 New Hampshire		31 New Jersey		32 New Mexico		33 New York		34 North Carolina		35 North Dakota		36 Ohio		37 Oklahoma		38 Oregon		39 Pennsylvania		40 Rhode Island		41 South Carolina		42 South Dakota		43 Tennessee		44 Texas		45 Utah		46 Vermont		47 Virginia		48 Washington		49 West Virginia		50 Wisconsin		51 Wyoming		52 Puerto Rico, Canal Zone, and Virgin Islands		53 Totals	54 Examined—Passed	55 Examined—Failed	56 % Failed	57 No. of Boards Examined by	Marginal Number
P	F	P	F	P	F	P	F	P	F	P	F	P	F	P	F	P	F	P	F	P	F	P	F	P	F	P	F	P	F	P	F	P	F	P	F	P	F	P	F	P	F	P	F	P	F	P	F	P	F	P	F						
												0	1	1	0			1	0																	4	0															13	12	1	7.7	8	49
														1	0																							2	0													6	5	1	16.7	3	50
														60	1																																					66	64	2	3.0	3	51
														74	2													1	0																							101	98	3	3.0	4	52
														44	0	1	0	1	0																																	60	58	2	3.3	9	53
												3	1					73	0																					0	1											90	86	4	4.4	6	54
												2	0					67	0					2	0																											78	76	2	2.6	7	55
												1	1					137	1					1	0									1	1																	158	154	4	2.5	9	56
																				149	0															0	1															159	156	3	1.9	7	57
1	0																					22	1	1	0											1	0					2	1									49	47	2	4.1	14	58
								10	0					4	0			2	0					66	0	1	0											3	0	1	0											106	102	4	3.8	13	59
								16	0	1	0	2	0	2	0			4	0					110	0									1	0					1	0											167	163	4	2.4	16	60
								10	0			0	1											85	0			1	0							1	1															123	120	3	2.4	15	61
								2	0			2	0	4	1			1	0					59	0									1	0									1	0					1	0	102	98	4	3.9	19	62
								1	0			1	0											17	0																			1	0	1	0					31	37	0	0.0	12	63
												1	0	2	0			2	0					61	0																											84	81	3	3.6	9	64
												2	2											2	0																									7	0	13	11	2	15.4	3	65
																												89	0																							93	93	0	0.0	2	66
												1	0																			144	0	1	0													1	0			216	214	2	0.9	12	67
												1	4	1	0									1	0							1	0																			77	73	4	5.2	10	68
																		1	0													46	0																			60	59	1	1.7	9	69
																																		88	2																	92	90	2	2.2	2	70
																																		135	6																	146	140	6	4.1	5	71
												2	1	1	0															1	0			63	7																	77	69	8	10.4	6	72
																		2	0	2	0															22	0					1	0									42	41	1	2.4	8	73
																																						10	0													13	12	1	7.7	2	74
								1	0			1	0																											63	2											76	74	2	2.6	5	75
								1	0																															79	5			18	0							119	114	5	4.2	7	76
												2	0	1	0	1	0					1	0	1	0							2	0	1	0							35	4									68	64	4	5.9	15	77
								1	0													3	0	1	0									1	0							1	0			48	0					73	72	1	1.4	13	78
												1	0					5	0					4	0																					39	0					82	82	0	0.0	12	79
																		1	0					1	0															0	1											12	11	1	8.3	6	80
																																																				7	7	0	0.0	2	81
												2	0			6	0	1	0					2	0					1	0															1	0					34	34	0	0.0	13	82
												2	1											2	0																											13	10	3	23.1	6	83
																								1	0																											7	6	1	14.3	5	84
										1	0	1	0											1	0									1	0																	11	10	1	9.1	8	85
																		2	0					1	0									1	0			2	0													19	19	0	0.0	9	86
												1	2					2	0					3	0															1	0											21	18	3	4.3	10	87
												4	0			2	0	3	0					7	0													3	0			1	1									36	35	1	2.8	12	88
																																																				5	3	2	40.0	3	89
												0	1					1	0																																	12	8	4	33.3	7	90
																																																				1	1	0	0.0	1	91
1	0	3	0			2	1	136	33	2	0	343	270	2	0	3	0	90	67			1	0	72	0	25	9			7	1	1	0	40	12					122	45	18	17	4	0	13	2			116	10	2,766	1,870	896	32.4	40	92
												0	2									1	0	2	0																									2	0	22	6	16	72.7	7	93
								2	1			30	17					101	4															3	2											5	0					185	155	30	16.5	11	94
3		124		0		5		227		4		761		214		14		593		151		34		529		39		94		13		201		393		34		30		330		86		27		119		4		140		8,996	..	..	..	..	95
3		123		0		4		193		4		442		210		14		521		151		33		529		30		94		12		201		360		32		30		275		62		27		117		4		130		..	7,834	..	..	..	96
0		1		0		1		34		0		319		4		0		72		0		1		0		9		0		1		0		33		2		0		55		24		0		2		0		10		..	..	1,162	12.9	..	97
0.0		0.8		0.0		20.0		14.9		0.0		41.9		1.9		0.0		12.1		0.0		2.9		0.0		23.1		0.0		7.7		0.0		8.4		5.9		0.0		16.7		38.7		0.0		1.7		0.0		7.1		..	..	..	..	..	98
27		28		29		30		31		32		33		34		35		36		37		38		39		40		41		42		43		44		45		46		47		48		49		50		51		52		53	54	55	56	57	

During 1959, there were 8,996 applicants for licensure by written examination; 7,834 of whom passed and 1,162 (12.9%) failed. The candidates examined represented 79 medical schools in the United States, including Puerto Rico; 12 approved medical schools of Canada; 244 faculties of medicine of foreign countries; 5 unapproved medical schools in the United States that are no longer in existence; and 7 schools of osteopathy. The Albert Einstein College of Medicine graduated its first class in 1959, but none of its graduates were examined for licensure in 1959. Osteopaths who were granted the privilege to practice medicine, surgery, or both by medical examining boards are included in these statistics. Osteopaths who obtain the legal right to special practice by other than medical examining boards are not included in these compilations.

Examination and reciprocity meetings are scheduled at frequent intervals by licensing boards in most of the states to facilitate licensure and enable physicians to commence the practice of medicine without undue delay. Later, in this study, there is included a tabulation giving the schedules for all states. The publication of the dates of examination and reciprocity or endorsement meetings is a regular biweekly feature of THE JOURNAL.

The 8,996 examinees included 5,845 graduates of approved medical schools in the United States; 178 graduates of approved medical schools in Canada; 2,766 graduates of 244 faculties of medicine located in countries other than the United States and Canada; 22 graduates of the unapproved medical schools in the United States which are no longer in existence, and 185 graduates of schools of osteopathy.

In table 3, as in table 1, the 8,996 physicians and others examined will not equal the number of persons licensed or added to the profession as given in succeeding tables, since a candidate tested in more than one state in a calendar year is counted in each state; however, if a candidate failed more than once in a given state within the year, he is counted in that state as a single failure. Figures showing the number of individual licentiates added to the medical profession in 1959 are given in tables 11, 12, and 13.

The greatest number of graduates from any one school to be examined was 216, representing a public university, the University of Tennessee College of Medicine. Of the graduates of this school, 144 were tested in Tennessee and 72 in 11 other states. The greatest number of graduates from a private school to be examined was 167, representing Jefferson Medical College; they were tested in 16 states. There were 110 of these examinees tested in Pennsylvania, where the school is located. Twenty-one schools, including those named, had more than 100 of their graduates examined for medical licensure in 1959, as follows:

	No. of Examinees	No. of States in Which Examinations Were Taken
Public Medical Schools		
Medical College of Georgia	102	2
Indiana University	169	4
State University of Iowa	109	11
Louisiana State University	120	3
University of Michigan	206	15
University of Minnesota	122	5
Ohio State University	158	9
University of Oklahoma	159	7
University of Tennessee	216	12
University of Texas	146	5
Medical College of Virginia	119	7
Private Medical Schools		
Emory University	115	3
Northwestern University	107	23
University of Louisville	100	7
Tulane University	153	9
St. Louis University	134	11
Duke University	101	4
Hahnemann Medical College	106	13
Jefferson Medical College	167	16
Temple University	123	15
University of Pennsylvania	102	19

Yale University and the State University of New York at Syracuse, with six examinees each; Boston University and Tufts University, with seven examinees each; and Albany Medical College, with eight examinees, had the fewest number of applicants for medical licensure by written examination before state boards. The majority of the graduates of these schools are licensed by endorsement of the certificate of the National Board of Medical Examiners. This is also true of other schools with small numbers of examinees.

There were 178 graduates of 12 approved medical schools in Canada tested for medical licensure in 1959 by 27 boards. The figures are given for each licensing board by school in table 3; the number examined by each board is given in table 4. Of these 178 candidates, 162 passed, and 16 (9.0%) failed.

Graduates of foreign faculties of medicine were examined by 38 boards. There were 2,766 examined; of these, 1,870 passed and 896 (32.4%) failed. Graduates of five unapproved medical schools were examined by seven states. There were 22 examined; of these, 6 passed, and 16 (72.7%) failed. Graduates of schools of osteopathy were tested in 11 states. Represented were 185 examinees; 155 passed, and 30 (16.2%) failed. Elsewhere (tables 11, 12 and 13) are given figures referring to actual licentiates and additions to the medical profession. Totals for the five categories are given in table 5.

Failures in Medical Licensure Examinations

During 1959 (as recorded in table 3), 1,162 of the 8,996 examinees for medical licensure failed. In table 6 are recapitulated the numbers examined in each state, the number who failed the examination, and the percentage of failures. Twenty states had no failures among their examinees; 11 states failed less than 5% of examinees; 4 boards failed from 5 to 10% of examinees; whereas failures in 17 states was more than 10% of those examined. It can be noted (table 3) that those states with high percentages of failures examine a considerable number of foreign-trained physicians and graduates of unapproved medical schools. The one exception is Florida. This state has no reciprocal provisions for medical licensure, and physicians planning semi-retirement in a more ideal climate seek licensure in this state. Many of these physicians have graduated from medical schools in the early years of the century and experience difficulty in writing examinations.

TABLE 4.—*Graduates of Medical Schools in Canada Examined for Licensure in the United States, 1959*

	Examined, No.	Passed, No.	Failed, No.
Alabama	1	1	0
Arizona	1	0	1
California	48	44	4
Colorado	1	1	0
Delaware	1	1	0
District of Columbia	2	2	0
Florida	3	2	1
Idaho	1	1	0
Illinois	3	3	0
Indiana	5	5	0
Kentucky	1	1	0
Maine	5	4	1
Maryland	3	3	0
Massachusetts	6	3	3
Michigan	17	17	0
Minnesota	16	16	0
New Mexico	1	1	0
New York	14	10	4
North Dakota	8	8	0
Ohio	10	10	0
Pennsylvania	18	18	0
South Dakota	1	1	0
Texas	2	2	0
Vermont	5	5	0
Virginia	2	1	1
Washington	2	1	1
Wisconsin	1	1	0
Totals	178	162	16

In general, state licensing boards require the applicant to receive an over-all average of 75% and at least 60% in any one subject. In case of failure in not more than two subjects, the applicant is permitted a second examination in those subjects, within 12 months. A few states consider such persons as conditioned in the subjects in which they fail. Conditioned candidates are not counted as failures in these statistics. When their grades are raised, after a successful examination, they are recorded among those who passed.

TABLE 5.—*Source of Candidates Examined for Licensure in the United States, 1959*

Medical Schools	No. of Schools	No. Examined	No. Passed	No. Failed	% Failed
Approved schools in United States	79	5,845	5,641	204	3.5
Approved schools in Canada	12	178	162	16	9.0
Foreign faculties of medicine	244	2,766	1,870	896	32.4
Unapproved medical schools	5	22	6	16	72.7
Schools of osteopathy	7	185	155	30	16.2
Totals		8,996	7,834	1,162	12.9

Of the 15,954 persons obtaining licenses in 1959, 539 failed state board tests before obtaining a license. Of these, 27 were graduates of approved schools in the United States, 2 were graduates of Canadian schools, and 510 were graduates of foreign faculties of medicine. Of the United States schools, 12 licentiates had one previous failure; 8, two; 3, three; 3, four; and 1 had five previous failures. The two Canadian graduates had one previous fail-

TABLE 6.—*Failures in Medical Licensure Examinations, 1959*

State in Which Examined	No. Examined	No. Passed	No. Failed	% Failures
Alabama	65	65	0	0.0
Alaska	3	3	0	0.0
Arizona	27	24	3	11.1
Arkansas	75	73	2	2.7
California	579	512	67	11.6
Canal Zone	1	1	0	0.0
Colorado	92	91	1	1.1
Connecticut	225	146	79	35.1
Delaware	18	16	2	11.1
District of Columbia	21	20	1	4.8
Florida	654	561	93	14.2
Georgia	272	270	2	0.7
Hawaii	34	28	6	17.6
Idaho	8	8	0	0.0
Illinois	778	536	242	31.1
Indiana	178	176	2	1.1
Iowa	102	102	0	0.0
Kansas	37	37	0	0.0
Kentucky	86	86	0	0.0
Louisiana	264	261	3	1.1
Maine	32	26	6	18.7
Maryland	250	223	27	10.7
Massachusetts	113	56	57	50.4
Michigan	323	322	1	0.3
Minnesota	193	193	0	0.0
Mississippi	112	112	0	0.0
Missouri	286	286	0	0.0
Montana	3	3	0	0.0
Nebraska	124	123	1	0.8
Nevada	0	0	0	0.0
New Hampshire	5	4	1	20.0
New Jersey	227	193	34	14.9
New Mexico	4	4	0	0.0
New York	761	442	319	41.9
North Carolina	214	210	4	1.9
North Dakota	14	14	0	0.0
Ohio	593	521	72	12.1
Oklahoma	151	151	0	0.0
Oregon	34	33	1	2.9
Pennsylvania	529	529	0	0.0
Puerto Rico	134	124	10	7.5
Rhode Island	39	30	9	23.1
South Carolina	94	94	0	0.0
South Dakota	13	12	1	7.7
Tennessee	201	201	0	0.0
Texas	393	360	33	8.4
Utah	34	32	2	5.9
Vermont	30	30	0	0.0
Virgin Islands	5	5	0	0.0
Virginia	330	275	55	16.7
Washington	86	62	24	38.7
West Virginia	27	27	0	0.0
Wisconsin	119	117	2	1.7
Wyoming	4	4	0	0.0
Totals	8,996	7,834	1,162	12.9

ure each. Of the 510 graduates of foreign faculties of medicine, 229 had one previous failure; 122 had two failures; 64 had three failures; 41 had four failures; 18 had five failures; and 36 had from six to sixteen failures—before obtaining a license. A few of the state boards have no restrictions on the number of examinations that may be taken prior to licensure; however, most states have a set limit of three examinations.

The following 13 approved schools in the United States and Canada had no failures among their graduates in medical licensing examinations last year:

	No. of Graduates Examined	No. of States in Which Examinations Were Taken
University of California, Los Angeles	44	2
University of California, San Francisco	81	3
Louisiana State University	120	3
University of Minnesota	122	5
University of Mississippi	63	3
University of Nebraska	80	6
Woman's Medical College of Pennsylvania	31	12
Medical College of South Carolina	93	2
Marquette University	82	12
University of British Columbia	7	2
University of Manitoba	34	13
University of Ottawa	19	9
University of Saskatchewan	1	1

Consolidated Results of Examinations

The combined results of two groups of examinations, the state medical board examinations and part 3 of the examinations of the National Board of Medical Examiners, are given in table 7. This table represents a comprehensive analysis of the performance of physicians from individual schools. It will be noted that in some instances schools having failures before state licensing boards had few, if any, failures before the National Board.

In 1959, there were 5,845 graduates of approved medical schools in the United States examined by state boards, 204 of whom failed (3.5%). In the same calendar year, 2,251 graduates of these schools were tested in the final examination of the National Board of Medical Examiners; nine failed. In both groups, a total of 8,096 were examined; 7,883 passed, and 213 (2.6%) failed.

Among the graduates of Canadian medical schools, 9.0% failed state board examinations whereas there were no failures among the 75 graduates who were tested by the National Board. There were no graduates of foreign medical faculties, unapproved medical schools, or schools of osteopathy examined by the National Board.

The total of all candidates examined by state boards was 8,996, 7,834 of whom passed and 1,162 (12.9%) failed. For both groups (state boards and the National Board), there were a total of 11,322 examined, with 10,151 successful candidates, and 1,171 failures (10.3%). Including figures for the National Board reduces the over-all percentage of failures by about 3%.

Registration by Reciprocity and Endorsement

The reciprocity and endorsement policies in medical licensure are summarized in table 8. Florida and the Virgin Islands do not have reciprocal relations with any state. Hawaii will endorse physicians certified by the National Board of Medical Examiners. Twenty-two boards require applicants for licensure to obtain a certificate from the board of examiners in the basic sciences of the state. In the section of this report pertaining to basic science boards is included a table outlining the reciprocity, endorsement, exemption, or waiver policies of the basic science boards.

Thirty-one boards have reciprocal agreements with specific states. In 19 states, the Canal Zone, and Guam, reciprocity is extended at the discretion of the licensing boards. Twenty states, which have reciprocal agreements, also have similar discretionary powers to endorse applicants from nonreciprocating states who meet the requirements of the board and who present credentials that correspond with those required by their respective states in the year issued. Also in this table is a column indicating the recognition afforded the certificate of the National Board of Medical Examiners.

Additional requirements, including professional practice, citizenship, oral examination and internship, and the fee for a license by reciprocity or endorsement are also recorded. In some states, physicians of Canadian birth are exempt from the citizenship requirement. This is indicated by a footnote. Few states will accept graduates of foreign faculties of medicine on a reciprocal basis. Other requirements or exemptions are indicated by footnote; footnote numbers are referred to in the "miscellaneous" column in the table.

This chart will be found helpful to physicians who are considering a change in location. The facts recorded in this table are intended merely to present statements of licensure policies. The information here given should be supplemented by direct communication with the licensing board. A list of the executive officers in charge of medical licensure appears elsewhere in this study.

The procedure for issuing licenses by reciprocity or endorsement varies. Some states entertain applications for licensure at any time; other hold monthly, quarterly, or semiannual meetings. (The policy in effect in each state is contained in table 24, which is presented later in this report.) In addition, The Journal publishes, biweekly, the exact dates when reciprocity or endorsement applications are considered.

TABLE 7.—*Combined Results of Examinations of State Boards and the National Board of Medical Examiners, 1959*

School	Results by Medical Examining Board Tests		Part 3 Examination of National Board of Medical Examiners		Total Examined	Totals		Failed, %
	P	F	P	F		P	F	
Medical College of Alabama	69	2	6	0	77	75	2	2.6
University of Arkansas	74	3	4	0	81	78	3	3.7
College of Medical Evangelists	60	6	47	0	113	107	6	5.3
University of California, Los Angeles	44	0	1	0	45	45	0	0.0
University of Southern California	67	1	16	0	84	83	1	1.2
Stanford University	43	2	18	1	64	61	3	4.7
University of California, San Francisco	81	0	3	0	84	84	0	0.0
University of Colorado	90	1	3	0	94	93	1	1.1
Yale University	4	2	71	0	77	75	2	2.6
Georgetown University	27	8	83	1	119	110	9	7.6
George Washington University	17	4	89	2	112	106	6	5.4
Howard University	70	17	20	0	107	90	17	15.9
University of Miami	68	1	36	1	106	104	2	1.9
Emory University	113	2	0	0	115	113	2	1.7
Medical College of Georgia	100	2	0	0	102	100	2	2.0
Chicago Medical School	12	1	69	0	82	81	1	1.2
Northwestern University	103	4	54	0	161	157	4	2.5
Stritch School of Medicine	59	5	29	1	94	88	6	6.4
University of Chicago	26	1	45	0	72	71	1	1.4
University of Illinois	86	4	83	0	173	169	4	2.3
Indiana University	165	4	1	0	170	166	4	2.4
State University of Iowa	107	2	4	0	113	111	2	1.8
University of Kansas	51	1	35	0	87	86	1	1.1
University of Louisville	97	3	16	0	116	113	3	2.6
Louisiana State University	120	0	0	0	120	120	0	0.0
Tulane University	149	4	0	0	153	149	4	2.6
Johns Hopkins University	64	3	18	0	85	82	3	3.5
University of Maryland	85	3	5	0	93	90	3	3.2
Boston University	6	1	61	0	68	67	1	1.5
Harvard Medical School	33	2	141	0	176	174	2	1.1
Tufts University	6	1	111	0	118	117	1	0.8
University of Michigan	201	5	7	0	213	208	5	2.3
Wayne State University	67	1	0	0	68	67	1	1.5
University of Minnesota	122	0	1	0	123	123	0	0.0
University of Mississippi	63	0	0	0	63	63	0	0.0
University of Missouri	34	1	2	0	37	36	1	2.7
Saint Louis University	128	6	25	0	159	153	6	3.8
Washington University	97	1	4	0	102	101	1	1.0
Creighton University	76	4	24	0	104	100	4	3.8
University of Nebraska	80	0	2	0	82	82	0	0.0
Albany Medical College	7	1	63	0	71	70	1	1.4
University of Buffalo	9	2	79	0	90	88	2	2.2
Albert Einstein College of Medicine	0	0	0	0	0	0	0	0.0
Columbia University	34	2	111	0	147	145	2	1.4
Cornell University	20	2	77	0	99	97	2	2.0
New York Medical College	17	3	114	0	134	131	3	2.2
New York University	13	4	129	0	146	142	4	2.7
State University of New York, New York	18	1	150	0	169	168	1	0.6
University of Rochester	12	1	71	1	85	83	2	2.4
State University of New York, Syracuse	5	1	67	0	73	72	1	1.4
University of North Carolina	64	2	0	0	66	64	2	3.0
Duke University	98	3	10	0	111	108	3	2.7
Bowman Gray School of Medicine	58	2	1	0	61	59	2	3.3
University of Cincinnati	86	4	2	0	92	88	4	4.3
Western Reserve University	76	2	27	0	105	103	2	1.9
Ohio State University	154	4	1	0	159	155	4	2.5
University of Oklahoma	156	3	0	0	159	156	3	1.9
University of Oregon	47	2	16	0	65	63	2	3.1
Hahnemann Medical College	102	4	8	0	114	110	4	3.5
Jefferson Medical College	163	4	13	0	180	176	4	2.2
Temple University	120	3	7	0	130	127	3	2.3
University of Pennsylvania	98	4	45	1	148	143	5	3.4
Woman's Medical College	31	0	18	0	49	49	0	0.0
University of Pittsburgh	81	3	1	0	85	82	3	3.5
University of Puerto Rico	11	2	21	0	34	32	2	5.9
Medical College of South Carolina	93	0	1	0	94	94	0	0.0
University of Tennessee	214	2	3	0	219	217	2	0.9
Meharry Medical College	73	4	3	0	80	76	4	5.0
Vanderbilt University	59	1	0	0	60	59	1	1.7
Southwestern Medical School	90	2	2	0	94	92	2	2.1
University of Texas	140	6	0	0	146	140	6	4.1
Baylor University	69	8	1	0	78	70	8	10.3
University of Utah	41	1	4	0	46	45	1	2.2
University of Vermont	12	1	39	0	52	51	1	1.9
University of Virginia	74	2	1	0	77	75	2	2.6
Medical College of Virginia	114	5	1	0	120	115	5	4.2
University of Washington	64	4	10	0	78	74	4	5.1
University of Wisconsin	72	1	5	0	78	77	1	1.3
Marquette University	82	0	7	1	90	89	1	1.1
Subtotals: U. S. Schools	5,641	204	2,242	9	8,096	7,883	213	2.6
University of Alberta	11	1	0	0	12	11	1	8.3
University of British Columbia	7	0	6	0	13	13	0	0.0
University of Manitoba	34	0	4	0	38	38	0	0.0
Dalhous	10	3	5	0	18	15	3	16.7
Queen's	6	1	1	0	8	7	1	12.5
Universi	10	1	2	0	13	12	1	7.2
Universi	19	0	3	0	22	22	0	0.0
University of Toronto	18	3	9	0	30	27	3	10.0
McGill University	35	1	45	0	81	80	1	1.2
Univers	3	2	0	0	5	3	2	40.0
Laval	8	4	0	0	12	8	4	33.3
Univer	1	0	0	0	1	1	0	0.0
Subtotals: Canadian Schools	162	16	75	0	253	237	16	6.3
	1,865	896	0	0	2,761	1,865	896	32.5
	6	16	0	0	22	6	16	72.7
	160	30	0	0	190	160	30	15.8
Subtotals: Others	2,031	942	0	0	2,973	2,031	942	3.1
Totals	7,834	1,162	2,317	9	11,322	10,151	1,171	10.3

TABLE 8.—*Reciprocity and Endorsement*

Marginal Number	The Examining Board of	Reciprocates with, or Endorses Certificates Granted by																														Marginal Number
		Alabama	Arizona	Arkansas	California	Colorado	Connecticut	Delaware	Dist. of Columbia	Florida	Georgia	Idaho	Illinois	Indiana	Iowa	Kansas	Kentucky	Louisiana	Maine	Maryland	Massachusetts	Michigan	Minnesota	Mississippi	Missouri	Montana	Nebraska	Nevada	New Hampshire	New Jersey	New Mexico	
1	Alabama	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	1
2	Alaska	+	..	+	+	+	+	..	+	..	..	..	..	+	..	+	+	..	..	+	..	+	+	+	+	..	..	+	+	+	..	2
3	Arizona	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	3
4	Arkansas	+	+	..	+	+	+	+	+	..	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	4
5	California	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	5
6	Canal Zone	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	6
7	Colorado	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	7
8	Connecticut	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	8
9	Delaware	..	..	..	..	..	..	..	+	..	..	+	+	+	..	+	..	+	+	+	+	+	..	..	..	..	..	..	+	..	..	9
10	District of Columbia	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	10
11	Florida	No reciprocity or endorsement policies											..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	11
12	Georgia	+	..	+	+	+	..	..	+	..	..	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	12
13	Guam	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	13
14	Hawaii	No reciprocal relations						..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	14
15	Idaho	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	15
16	Illinois	+	..	+	+	+	+	..	..	..	+	..	..	+	+	+	+	+	..	+	..	+	+	+	+	+	+	+	..	+	..	16
17	Indiana	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	17
18	Iowa	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	18
19	Kansas	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	19
20	Kentucky	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	20
21	Louisiana	+	+	+	+	+	+	+	+	..	+	+	+	+	+	+	+	..	+	+	+	+	+	+	+	+	+	+	+	+	+	21
22	Maine	..	+	+	+	+	+	+	+	..	+	..	..	+	+	+	+	+	..	..	+	+	+	+	+	+	+	+	+	+	+	22
23	Maryland	+	..	+	+	..	+	+	+	..	+	+	+	+	+	+	+	+	..	..	+	+	+	+	+	+	+	+	+	+	+	23
24	Massachusetts	+	..	+	+	..	+	+	+	..	+	+	..	+	+	+	+	+	+	+	..	..	+	+	+	+	+	..	+	+	..	24
25	Michigan	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	..	+	+	+	+	+	+	+	+	+	25
26	Minnesota	+	+11	+	+	+	+11	+	+	..	+	+11	+	+11	+	+11	+11	+	+	+	..	+	..	+	+	+	+	+	+11	+	+	26
27	Mississippi	+	+	+	+	+	+	+	+	..	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	27
28	Missouri	+	+	+	+	+	+	+	+	..	+	+	+	+	+	+	+	+	+	+	+	+	+	+	..	+	+	+	+	+	+	28
29	Montana	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	29
30	Nebraska	+	+	+	+	+	+	+	+	..	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	..	+	+	+	+	30
31	Nevada	+	+	+	+	+	+	+	+	..	+	+	+	+	+	+	+	+	+	+	..	+	+	+	+	+	+	+	+	+	+	31
32	New Hampshire	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	32
33	New Jersey	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	..	+	33
34	New Mexico	+	+	+	+	+	+	+	+	..	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	..	34
35	New York	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	35
36	North Carolina	+	+	+	+	+	+	+	+	..	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	36
37	North Dakota	+	..	+	+	+	..	+	..	..	+	+	+	+	+	+	+	+	+	..	..	+	+	..	+	+	+	+	+	+	+	37
38	Ohio	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	38
39	Oklahoma	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	39
40	Oregon	+	+	+	+	+	+	+	..	..	+	+	+	+	+	..	+	+	+	+	..	+	+	+	+	+	+	+	+	+	+	40
41	Pennsylvania	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	41
42	Puerto Rico	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	+	..	..	+	..	+	..	..	..	..	42
43	Rhode Island	+	+	+	+	+	+	+	+	..	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	43
44	South Carolina	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	44
45	South Dakota	+	+	+	+	..	+	+	+	..	+	+	+	+	+	+	+	+	+	..	..	+	+	+	+	+	+	+	..	+	+	45
46	Tennessee	+	+	+	+	+	+	+	+	..	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
47	Texas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
48	Utah	+	+	+	+	+	+	+	+	..	+	+	+	+	+	+	+	+	+	+	+	+	..	+	+	+	+	+	+	+	+	48
49	Vermont	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	49
50	Virginia	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
51	Virgin Islands	No reciprocal relations						..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	51
52	Washington	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	52
53	West Virginia	+	..	+	20	20	+	+	+	..	+	..	+	20	20	20	20	+	+	+	20	+	+	+	+	+	+	+	..	+	..	53
54	Wisconsin	+	+	+	+	+	+	+	+	..	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	54
55	Wyoming	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	55

This summary should be supplemented by direct communication with the secretary of

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Some states have additional requirements for graduates of schools outside the United States and Canada.

+ indicates reciprocal or endorsement relationships have been established; .. indicates no reciprocal *or endorsement* relationships have been established. (See column—"At the *discretion of the* board.")

1. D. Declaration of Intention of citizenship. ⊕ in citizenship column indicates full citizenship required; in other columns it implies a requirement.
2. In most cases there is a small additional recording or registration fee.
3. Year of practice after licensure *required.*
4. Internship accepted in lieu of one year's practice.
5. Two years' professional practice required.
6. All applicants must be graduates of a medical school approved by the American Medical *Association.*
7. Just preceding application.
8. *Not required* if applicant has been in practice more than 5 years.
9. Basic science certificate required either by reciprocity or examination in addition to basic science subjects of National Board.
10. Canadian citizens are required to file first papers.
11. Not applicable to *citizens of Canada.*
12. Oral examination required when application is based on a license dated five or more years prior to filing *application.*
13. Must be residents of the Canal Zone or Republic of Panama.
14. Oral examination required.
15. Endorsement of National Board of Medical Examiners, $35.
16. Active practice for a period of not less than three years immediately *preceding* date of application.
17. Practical clinical *examination required.*
18. In lieu of its own examination, certificate of National Board may be accepted in whole or in part.
19. Minimum fee.
20. *Licentiates* of California, Colorado, Indiana, Iowa, Kansas, Massachusetts, New York, and Rhode Island accepted on reciprocal basis at discretion of board.
21. Not required if country in which applicant is licensed will admit to practice citizens of the United States licensed to practice in some state or on proof of requirements similar to those required by California for graduates of *foreign medical schools.*
22. At discretion of Health Director.

The credentials presented by physicians granted licenses to practice medicine without written examination are given in table 9. There were 8,234 so registered on the basis of licenses from other states, the District of Columbia, the possessions of the United States, Canada and foreign countries, the certificate of the National Board of Medical Examiners, and by acceptance of service with an agency of the government of the United States. California issued the greatest number of licenses by this method. In this state, 1,732 were registered. New York licensed 1,169 by this method. Figures for other states were fewer than 400. Eight states licensed more than 200.

Policies of Medical Licensing Boards

Reciprocates with, or Endorses Certificates Granted by																							Requirements							
Marginal Number	New York	North Carolina	North Dakota	Ohio	Oklahoma	Oregon	Pennsylvania	Rhode Island	South Carolina	South Dakota	Tennessee	Texas[6]	Utah	Vermont	Virginia	Washington	West Virginia	Wisconsin	Wyoming	Alaska	Puerto Rico	At the Discretion of the Board	National Board of Medical Examiners	Basic Science Certificate	Internship	Professional Practice	Citizenship	Fees, Dollars	Miscellaneous	Marginal Number
1	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	+	+	..	⊖	1[4]	⊖[11]	50	..	1
2	..	+	+	+	+	+	..	..	..	..	+	+	+	+	+	+	+	+	..	..	..	..	+	⊖	⊖	0	⊖	110	6	2
3	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	+	+	⊖	⊖	1[6]	D	100	45	3
4	..	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	..	..	..	⊖	..	1[4]	⊖	100	38	4
5	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	+	+[25]	..	⊖	0	⊖[21]	100	12	5
6	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	+	+[22]	..	⊖	2	..	5	13	6
7	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	+	+[9]	⊖	⊖	..	⊖	50	42	7
8	..	..	..	+	..	..	+	+	..	..	+	+	..	+	..	..	+	..	..	..	..	+	+	⊖[5]	..	3[16]	D[10]	100	42	8
9	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	+	+[5]	..	⊖	2	⊖	100	47	9
10	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	+	+[27]	⊖[32]	⊖	1[3]	..	50	..	10
11	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	⊖	..	..	⊖	..	..	11
12	..	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	..	..	+	..	..	..	..	0	⊖	50	..	12
13	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	+	+	..	⊖	0	..	50	46, 6	13
14	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	+	..	⊖	..	D	50	27, 42, 6	14
15	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	+	+	..	⊖	..	D	100	..	15
16	..	+	+	+	+	+	+	+	..	+	+	+	+	+	+	+	+	+	+	+	..	..	+[17]	..	⊖	1	⊖	100	17, 42	16
17	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	+[35]	..	..	..	1[4]	..	25	..	17
18	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	+	+	⊖	⊖	1[4]	D	50	39, 6	18
19	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	+	+	⊖	⊖	1[4, 7]	⊖	[28]	29, 42	19
20	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	+	+	..	⊖	..	⊖	75	42	20
21	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	..	..	..	..	..	⊖	1[4]	⊖[10, 40]	50[28]	42	21
22	..	+	+	+	+	+	+	+	+	+	+	+	+	+	+	..	+	+	+	..	..	..	+	..	⊖	1[4]	D	52	..	22
23	+	+	..	+	+	+	+	+	+	..	+	+	..	+	+	..	+	+	..	+	+	+	+	..	..	1[4]	D	100	42	23
24	+	+	..	+	+	..	+	+	+	..	+	+	+	+	+	..	+	+	..	..	..	+	+	..	..	0	D	75	..	24
25	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	..	⊖[37]	⊖	1[4]	⊖	100	34	25
26	+[41]	+	..	+[41]	+	+	+	+[41]	..	+	+	+	..	+	+	+	+	+	+	+	..	+	+	⊖	..	0	⊖	100	11, 17, 42	26
27	..	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	..	+	+	..	..	..	⊖	50	42	27
28	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+[27]	..	⊖[33]	1[4]	⊖	100	42	28
29	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	+	+	..	..	1[4]	⊖	75	14, 42	29
30	+	+	+	+	+	+	+	..	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	⊖	..	1[4]	⊖	50[28]	..	30
31	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	..	..	+	⊖	⊖	1[4]	⊖	200	14, 42	31
32	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	+	+	..	⊖	0	⊖[11]	50	..	32
33	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	..	..	+	+	..	⊖	0	⊖	100	..	33
34	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	⊖	..	1[4]	D	50	..	34
35	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	+	+	..	..	2	D	40	..	35
36	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	..	..	+	..	..	..	0	⊖	100	29, 6	36
37	..	+	..	+	+	+	+	..	+	+	..	+	+	+	+	+	+	+	+	+	+	+	+	..	⊖	1	D[11]	50	14, 42	37
38	+	+	+	..	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	..	+	+	..	..	1	⊖	100	..	38
39	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	+	+	⊖[32]	⊖	1[4]	⊖	100	6	39
40	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	..	+	+[9, 27]	⊖	⊖	..	D	100	6, 42	40
41	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	+	+	..	⊖	2[24]	D	50	42	41
42	..	..	+	..	..	..	..	..	+	..	..	..	..	..	..	..	..	+	..	..	..	+[3, 39]	+	..	⊖	1[3]	⊖	30	..	42
43	..	+	+	+	+	+	+	..	+	+	+	+	+	+	+	+	+	+	+	+	..	+[14]	+[14]	⊖	⊖	0	D	20	14	43
44	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	..	⊖	1[4]	⊖	100	42	44
45	+	+	+	+	+	+	+	+	+	..	+	+	+	+	+	+	+	+	+	..	..	..	+	⊖	⊖	1	D	50	..	45
46	+	+	+	+	+	+	+	+	+	+	..	+	+	+	+	+	+	+	+	..	..	+	+[30]	⊖	..	0	⊖	50	42	46
47	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	⊖	..	0	D	100	42	47
48	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	..	..	+	+	..	⊖	[31]	..	50	42	48
49	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	+	+	..	⊖	1[4]	⊖	50	11	49
50	+	+	+	+	+	+	+	+	+	+	+	+	+	+	..	+	+	+	+	+	+	+[39]	+	..	..	2[26]	D[11]	100	42	50
51	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	⊖	..	..	65	42	51
52	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	+	+	⊖	⊖	0	..	50	..	52
53	20	+	+	+	+	+	+	20	+	+	+	+	+	+	+	..	..	+	+	+	+	..	+	..	⊖	0	⊖	100	..	53
54	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	..	+	+	+	+[14]	+[18]	⊖	⊖	..	D	100[9]	6	54
55	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	+[14]	+[14]	..	⊖	0	⊖	50	..	55

the licensing board of the state in which the physician is interested. See page 413.

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23. Oral examination required if applicant's state requires it.
24. If the applicant passes the examination in the state from which he transfers after the completion of his internship, no practice is required.
25. May require oral examination.
26. Internship accepted at the discretion of the board as the equivalent of two years' practice.
27. Residence for one year required.
28. Fee same as applicant's state charges but not less than $50.
29. Graduates of foreign medical schools are accepted at the discretion of the board.
30. Diplomates of National Board not required to have been in practice for three years.
31. Same as required of candidates of state applying for licensure.
32. Not required for licensure by reciprocity.

[illegible] required in certain cases when accept- [illegible] whom reciprocal relations have not been established.

35. Must meet requirements of the board and holds a valid license obtained by written examination.
36. Fee same as applicant's state charges but not less than $75.
37. For matriculants after Oct. 15, 1937.
38. Graduates of foreign schools not accepted.
39. Reciprocity extended at discretion of board to candidates whose qualifications would entitle them to admission to examination and who took examination equivalent to that required by this board.
40. Permanent license withheld until completion of citizenship.
41. At the discretion of the board.
42. Graduates of foreign medical schools are not accepted for licensure by reciprocity.
43. Reciprocity extended at discretion of board to states having comparable licensing requirements and which accept Colorado applicants on a substantially equal reciprocal basis.
44. Consecutive years immediately preceding application.
45. Graduates of medical schools in Canada and foreign medical graduates are not accepted for licensure by reciprocity.

The largest number of candidates who presented the same type of credentials were the 3,377 diplomates certified by the National Board of Medical Examiners; 952 were licensed in New York; 659, in California; and 307, in Massachusetts. Other states registered fewer than 200. None were licensed in Arkansas, Florida, Indiana, Louisiana, North Carolina, South Dakota, and Texas.

There were 359 licenses issued in Pennsylvania, 349 in Michigan, 334 in Ohio, and 301 in Missouri, which were presented to other states for reciprocal registration. More than 250 licenses from Illinois and Maryland were endorsed for reciprocal licensure. Licenses from every state were used as the basis for registration by this method, ranging from

TABLE 9.—*Candidates Licensed by Reciprocity and Endorsement of Credentials by States, 1959*

States Issuing Licenses by Reciprocity or Endorsement	Alabama	Alaska	Arizona	Arkansas	California	Colorado	Connecticut	Delaware	District of Columbia	Florida	Georgia	Hawaii	Idaho	Illinois	Indiana	Iowa	Kansas	Kentucky	Louisiana	Maine	Maryland	Massachusetts	Michigan	Minnesota	Mississippi	Missouri	Montana	Nebraska	Nevada	New Hampshire	New Jersey	New Mexico	New York	North Carolina	North Dakota	Ohio	Oklahoma	Oregon	Pennsylvania	Rhode Island	South Carolina	South Dakota	Tennessee	Texas	Utah	Vermont	Virginia	Washington	West Virginia	Wisconsin	Wyoming	U. S. Govt. Services	National Board of Medical Examiners	Canal Zone, Puerto Rico	Canadian and Foreign	Total Licensed
Marginal Number	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40	41	42	43	44	45	46	47	48	49	50	51	52	53	54	55	56
Alabama	..	..	..	3	1	..	..	..	..	..	9	..	..	..	1	..	..	1	10	..	..	..	..	..	5	1	..	..	..	..	..	..	2	3	..	2	..	..	3	..	..	..	15	2	..	..	2	..	..	..	..	..	12	..	..	72
Alaska	..	..	..	1	1	..	..	..	..	..	..	..	..	1	..	1	..	..	..	..	2	..	1	2	..	..	..	..	..	..	..	..	..	..	..	1	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	9	..	..	19
Arizona	1	..	..	..	5	5	..	..	1	3	1	..	..	4	3	10	4	..	5	..	1	..	10	7	1	3	..	6	..	..	..	..	3	..	..	7	1	..	2	..	..	..	4	5	..	..	3	1	..	5	..	..	20	..	..	121
Arkansas	..	..	..	..	1	..	..	..	..	..	1	..	..	3	..	..	3	..	5	..	..	..	..	1	..	2	..	..	..	..	..	..	..	..	..	..	1	..	..	..	..	..	6	5	..	..	..	..	..	1	..	..	..	..	..	29
California	5	..	2	7	..	26	3	..	3	16	29	2	..	89	44	49	29	15	40	3	50	2	84	60	2	81	1	33	1	..	7	..	30	18	5	104	11	13	63	..	5	1	21	38	8	2	10	12	3	42	1	..	659	..	..	1,732
Colorado	..	..	1	1	1	..	..	..	..	..	1	..	1	3	2	2	2	..	2	..	1	..	8	5	..	13	1	11	..	..	..	1	2	1	..	11	5	..	7	..	..	1	3	8	..	..	..	2	..	4	..	..	26	..	..	126
Connecticut	1	..	1	1	4	..	..	..	1	..	1	..	..	1	1	..	1	1	2	2	7	..	2	1	..	2	..	..	..	..	1	..	10	1	..	1	..	..	4	..	..	..	1	1	..	..	1	..	..	1	..	..	189	..	..	239
Delaware	..	..	..	..	..	..	1	..	..	..	..	..	..	..	..	..	..	..	..	..	2	..	..	..	..	1	..	..	..	..	2	..	..	1	..	..	..	..	5	..	..	..	..	..	..	..	1	..	..	..	..	..	2	..	..	15
District of Columbia	1	..	..	1	..	3	1	..	..	..	..	..	..	..	..	..	..	1	..	1	22	1	1	2	..	3	..	..	..	2	1	..	7	3	..	10	1	..	5	..	..	..	3	..	..	..	..	..	1	1	..	..	78	..	18	167
Florida	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	....
Georgia	..	..	..	1	..	..	..	..	..	..	..	..	..	4	2	1	1	2	8	1	5	..	3	1	3	2	..	..	..	..	1	..	..	13	..	4	..	..	3	..	9	..	16	1	..	1	2	..	2	..	..	1	4	..	..	91
Hawaii	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	26	..	..	26
Idaho	..	..	..	..	2	1	..	..	..	..	..	..	..	1	..	1	3	..	2	..	1	..	..	2	..	3	..	1	..	..	..	..	..	..	..	2	1	3	1	..	..	..	1	..	2	..	..	3	..	..	..	..	10	..	..	40
Illinois	..	..	1	3	4	..	..	..	..	..	1	..	..	..	8	1	2	1	1	..	4	1	6	..	..	6	..	3	..	..	1	..	2	1	2	12	2	..	6	..	..	..	1	1	1	..	1	..	..	11	..	2	128	..	..	219
Indiana	1	..	..	..	9	1	3	..	1	..	4	..	..	36	..	4	1	19	2	1	1	..	13	3	3	16	1	5	..	..	..	1	3	4	..	27	..	..	10	3	..	1	4	3	..	..	2	2	2	5	..	..	..	..	3	197
Iowa	..	..	..	..	4	..	..	..	..	..	1	..	..	4	2	..	1	1	3	..	5	..	4	5	..	3	..	13	..	..	1	..	..	1	..	5	..	..	7	..	..	1	3	..	..	1	2	1	..	5	..	..	7	..	5	85
Kansas	..	..	..	1	1	2	..	..	..	..	..	..	..	3	3	1	..	6	1	..	..	..	..	..	..	5	..	5	..	..	..	..	2	..	..	5	3	..	1	..	..	..	1	3	..	..	2	1	..	3	..	..	14	..	..	63
Kentucky	..	..	..	..	1	1	..	..	..	..	2	..	..	2	4	..	1	..	4	1	..	1	3	..	4	3	..	..	..	..	..	..	2	2	..	4	1	..	7	..	1	..	15	..	..	1	2	2	3	2	..	..	21	..	..	90
Louisiana	4	..	..	7	3	2	..	..	..	..	15	..	..	1	1	1	..	2	..	1	3	1	7	1	17	5	..	2	..	..	..	..	2	5	..	2	4	..	3	..	2	..	7	11	..	..	5	..	..	..	..	..	..	..	..	114
Maine	..	..	1	..	2	..	1	..	1	..	..	..	..	..	..	..	..	..	1	..	..	3	1	..	..	..	..	..	..	..	1	1	..	..	..	2	..	..	2	1	..	..	..	1	..	..	..	..	..	1	..	..	25	..	..	44
Maryland	1	..	..	1	10	2	..	..	12	..	6	..	..	1	3	1	2	..	1	..	..	2	2	..	1	4	..	1	..	..	2	..	1	2	..	3	2	..	15	..	..	..	2	6	..	1	7	..	..	1	..	..	65	..	..	157
Massachusetts	1	..	..	1	9	..	1	..	..	..	1	..	..	..	3	..	1	3	2	2	16	..	..	1	1	3	..	1	..	..	2	..	7	4	..	7	1	..	12	2	1	..	2	1	..	3	1	..	..	4	..	..	307	..	..	406
Michigan	1	..	..	..	9	4	1	..	..	1	1	..	..	17	17	12	1	4	1	..	12	3	..	6	1	7	..	..	..	1	2	..	3	3	..	26	..	..	4	1	..	..	5	6	..	..	6	..	2	12	..	..	20	..	..	189
Minnesota	1	..	..	7	6	1	..	..	..	..	..	..	..	4	7	9	1	..	2	..	4	..	11	..	..	10	..	9	..	..	..	..	..	1	..	3	2	1	9	..	..	..	2	6	..	..	6	1	1	6	..	..	67	..	..	177
Mississippi	..	..	..	..	1	..	..	..	..	..	1	..	..	..	1	..	..	2	6	..	1	..	1	..	..	1	..	..	..	..	..	..	..	1	..	..	..	..	..	..	1	..	8	..	..	..	..	..	..	..	..	..	5	..	2	31
Missouri	..	..	..	5	3	2	..	1	..	..	4	..	..	6	..	3	26	..	2	..	4	..	2	3	3	..	..	5	..	..	1	..	1	1	..	3	2	..	2	..	1	..	4	4	1	..	1	..	..	1	..	..	30	..	..	121
Montana	..	..	..	..	3	2	..	..	..	..	..	..	..	2	1	2	2	..	1	..	..	..	2	3	..	3	..	3	..	..	..	..	2	..	1	1	1	..	1	..	..	..	..	2	..	..	1	2	..	1	..	..	10	..	..	46
Nebraska	..	..	..	..	2	2	..	..	..	..	..	..	..	..	1	2	..	..	3	..	..	..	1	1	..	..	..	..	..	..	..	..	..	..	1	1	..	..	..	..	..	2	..	..	..	..	1	..	..	2	..	..	1	..	..	20
Nevada	..	..	1	..	6	..	..	..	..	..	..	..	..	3	..	1	1	..	..	..	..	..	1	1	..	..	..	2	..	..	..	..	1	..	..	..	..	1	4	..	..	..	1	2	1	..	..	1	1	..	..	..	4	..	..	32
New Hampshire	..	..	..	..	..	..	1	..	..	1	..	..	..	..	1	..	..	..	..	..	..	1	1	..	..	..	..	2	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	2	1	..	..	..	..	..	23	..	3	36
New Jersey	..	..	..	..	1	1	..	..	..	5	2	..	..	2	..	1	2	5	6	3	12	1	3	1	..	20	1	1	..	..	..	..	44	3	..	11	1	..	65	7	1	..	3	..	..	..	3	1	..	..	..	..	180	..	..	386
New Mexico	..	..	1	1	3	6	..	..	..	..	..	..	..	2	3	..	4	1	1	..	1	..	2	4	..	5	..	2	..	..	1	..	3	..	..	5	4	..	2	1	..	2	3	7	1	1	..	..	..	..	..	..	5	..	..	71
New York	2	..	..	..	15	4	1	1	2	..	1	..	..	3	6	2	..	6	6	..	25	1	15	9	2	3	..	5	..	..	10	..	..	14	..	3	..	..	38	..	..	..	13	3	..	2	12	1	2	4	..	..	952	4	2	1,169
North Carolina	2	..	..	1	5	..	..	..	..	..	8	..	..	5	..	..	1	1	4	..	7	..	1	..	1	1	..	1	..	..	..	..	4	..	..	1	..	..	6	..	5	..	3	4	..	1	10	..	2	1	..	..	..	..	..	75
North Dakota	..	..	..	..	2	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	1	..	1	..	1	1	..	1	..	..	..	..	..	..	..	1	..	..	3	..	..	..	..	..	..	..	..	1	1	..	..	..	3	..	..	16
Ohio	..	..	..	1	9	2	15	..	2	2	4	..	..	25	14	4	1	9	4	5	23	3	19	3	..	20	..	2	..	..	8	1	14	2	..	..	1	1	27	6	..	1	4	4	2	1	18	..	8	6	..	..	81	5	..	360
Oklahoma	..	..	..	4	..	1	..	..	1	..	2	..	..	2	1	1	3	..	1	..	3	..	1	3	..	6	..	1	..	..	..	..	..	..	..	1	..	..	1	..	..	..	5	5	..	..	..	..	..	2	..	..	5	..	..	49
Oregon	..	..	1	..	13	3	..	..	..	..	1	..	1	2	1	4	3	1	2	..	1	..	7	13	..	2	1	3	..	..	..	1	..	1	..	4	..	..	1	..	..	..	1	1	1	..	..	2	..	1	..	..	24	..	..	96
Pennsylvania	..	..	..	..	4	4	1	..	..	1	3	..	..	6	3	1	1	1	3	4	19	..	9	2	..	5	..	2	..	..	4	..	3	7	1	14	2	1	..	..	3	1	2	4	..	..	6	..	1	5	..	2	130	1	..	256
Rhode Island	..	..	..	..	..	..	1	..	..	..	..	..	..	..	..	..	..	..	..	..	1	1	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	1	..	..	..	..	1	..	..	..	..	..	..	..	..	27	..	..	32
South Carolina	..	..	..	..	..	1	..	..	..	..	6	..	..	1	1	..	..	..	1	..	3	..	..	1	..	..	..	..	..	..	..	..	2	8	..	3	..	..	3	..	..	..	1	..	..	1	1	..	..	..	..	..	9	..	..	42
South Dakota	..	..	..	..	1	1	..	..	..	..	..	..	..	2	..	3	1	..	1	..	..	..	1	7	..	..	2	1	..	..	..	..	1	..	..	2	..	..	..	..	..	..	..	..	..	..	1	..	..	3	..	..	..	..	..	27
Tennessee	..	..	..	1	4	..	..	..	1	..	12	..	..	1	2	..	..	6	5	..	3	..	4	..	25	3	..	..	..	..	1	..	3	4	..	4	..	..	5	..	..	..	..	..	..	..	6	..	..	1	..	..	9	..	..	100
Texas	1	1	..	19	8	3	1	..	2	4	8	..	1	15	..	3	4	10	19	..	10	..	7	6	7	40	1	3	..	..	1	..	9	2	1	13	7	..	10	..	..	..	9	..	1	..	8	1	1	7	..	1	..	1	..	215
Utah	..	..	1	1	14	1	..	..	..	..	1	1	2	3	2	2	..	..	2	..	3	..	..	..	..	..	..	..	..	..	..	..	2	1	..	2	1	..	1	..	2	..	2	3	..	..	..	..	1	1	..	2	19	..	..	71
Vermont	..	..	..	..	1	..	..	..	..	..	..	..	..	..	..	..	..	..	2	..	1	..	..	..	..	..	..	..	..	..	..	..	..	1	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	9	..	..	14
Virginia	1	..	..	..	2	..	..	..	4	1	2	..	..	1	1	1	..	1	3	1	11	..	2	1	..	1	..	..	..	..	..	..	5	5	..	3	..	..	7	..	4	1	6	1	..	..	..	..	4	1	..	..	58	..	..	128
Washington	..	..	..	1	14	3	..	..	1	..	1	..	2	5	..	8	3	..	..	..	1	..	9	8	..	7	..	8	..	..	..	..	4	..	..	7	..	4	2	..	..	1	4	6	4	..	8	..	..	3	..	..	40	..	13	163
West Virginia	..	..	..	3	..	..	..	..	..	..	1	..	..	2	..	1	2	1	2	1	3	..	..	..	3	2	..	1	..	..	..	..	3	3	..	10	..	..	7	..	4	..	3	1	..	..	8	..	..	1	..	..	15	..	..	77
Wisconsin	..	..	..	..	6	5	1	..	..	..	..	..	..	8	3	3	2	1	2	..	5	..	2	9	1	9	..	4	..	..	1	..	1	..	2	7	..	1	1	..	..	1	..	2	..	..	1	..	1	..	..	10	23	..	..	112
Wyoming	..	..	..	..	3	2	..	..	..	..	..	..	..	..	..	..	..	..	2	..	1	..	1	1	..	..	..	2	..	..	..	..	1	..	..	..	..	..	..	..	..	..	..	1	..	..	..	..	..	1	..	..	2	..	..	17
Canal Zone, and Puerto Rico	..	..	..	..	..	..	..	..	..	1	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	5	..	..	..	..	..	3	..	..	..	..	..	..	..	..	..	..	..	..	..	21	..	..	30
Totals	23	1	10	72	193	91	32	2	32	35	130	3	7	270	142	138	169	101	168	28	277	23	219	171	81	301	8	137	1	3	17	6	181	116	13	331	51	25	350	22	39	13	187	150	22	17	131	34	30	145	1	18	3,377	11	40	8,244
Marginal Number	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40	41	42	43	44	45	46	47	48	49	50	51	52	53	54	55	56

1 each from Alaska, Nevada, and Wyoming to 359 from Pennsylvania.

Six states registered 18 physicians by endorsement of credentials from one of the government services. Eleven physicians were licensed by four boards on the basis of a license issued in the Canal Zone and Puerto Rico; 46 physicians were licensed by 7 boards on the basis of Canadian or foreign credentials.

Table 10 records the number of individual schools represented by the 8,234 reciprocity licentiates. Every approved medical school in the United States, and the University of Puerto Rico were represented with the exception of the Albert Einstein College of Medicine which while graduating a class in 1959 did not have any of its graduates licensed during the year. All but one of the approved Canadian schools were so registered. The 8,234 licentiates included 7,589 graduates of approved schools in the United States and 165 from Canadian medical schools. Licenses without written examination were obtained by 289 foreign-trained physicians. Twenty-seven graduates of approved medical schools no longer in operation were registered, 12 graduates of unapproved medical schools, and 152 graduates of schools of osteopathy.

This table reflects the movement of graduates to states other than those in which they obtained their professional training or in which they first established their practice.

Licentiates Representing Additions to the Medical Profession

Figures for the number of physicians who secured their first license to practice medicine and surgery in 1959 and who, therefore, represent additions to the medical profession in the United States and its possessions are presented in tables 11 and 12. Included in these compilations are figures pertaining to candidates examined and licensed in 1959; candidates who were examined in previous years but to whom licenses were not issued until 1959, pending completion of a required internship, citizenship, or other technicality; and physicians not previously licensed in any state but who were certified during the year on the basis of the certificate of the National Board of Medical Examiners. The figures also include the number of physicians licensed on the basis of government credentials and Canadian and foreign licenses. The majority represent recent graduates.

The official figures indicate that 8,269 persons were added to the physician population in 1959 in the United States, the District of Columbia, the Canal Zone, Puerto Rico, and the Virgin Islands. In 1959, there were about 3,500 deaths of physicians reported to the office of the American Medical Association. When this figure is deducted from the number licensed in 1959 for the first time, it will be seen that the net increase in the physician population in the United States and its possessions was 4,769. This was an increase of 660 over the number so added to the physician population in the preceding year.

In analyzing table 11, it can be noted that New York had the greatest number of first licentiaties (1,121). Three other states added more than 500 to their physician population: namely, California (676), Illinois (521), and Pennsylvania (530). Increases, as compared with 1958,[2] occurred in 29 states. None were added in Delaware and Nevada. The most notable increases were in Alabama, Connecticut, Illinois, New Jersey, Puerto Rico, South Carolina, and Tennessee. There was no marked decrease evident in any state.

The 8,269 licentiates representing additions to the medical profession in the last calendar year included 6,490 who secured their licenses by written examination and 1,779 by endorsement of credentials. The latter were mainly physicians holding the certificate of the National Board of Medical Examiners and using the certificate as the basis of licensure by endorsement of credentials.

Increases in the physician population arranged in nine geographical divisions in the United States are shown in table 12. The Middle Atlantic, East North Central, and South Atlantic groups had the greatest number of first licentiates—1,829; 1,547; and 1,264, respectively. More than 400 were added in five other groups—New England (533), West North Central (795), East South Central (537), West South Central (694), and Pacific (826). The Mountain states added 109, and the possessions added 135.

In the past 25 years (1935-1959), 166,160 physicians have been added to the medical profession, as determined by the number who received licenses for the first time. Figures for each year during this period are presented in table 13. Of the 166,160 additions, 137,742 were licensed after a successful written examination and 28,418 by reciprocity or endorsement of credentials. The total number of licenses issued in the same period was 298,440.

Registration of Physicians, 1904-1959

A recapitulation of totals, for 1959 and for all previous years since 1904, is included in table 14. This tabulation includes for each year the number of physicians examined and registered by written examination, the annual percentage of failures, the number registered annually by reciprocity or endorsement of credentials, and the total registered. The total number of physicians registered from 1904 to 1933 remained somewhat constant except, in 1918, when 4,231 were licensed—the lowest registration in 56 years. This decrease was due to a sudden withdrawal of physicians from civilian life in World War I.

After 1933, there was an upward trend for a time, followed by a decline in the years 1940 to 1942, inclusive. There was a noticeable increase in

TABLE 10.—*Candidates Licensed by Reciprocity and*

	Marginal Numbers	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
Marginal Number	School	Alabama	Alaska	Arizona	Arkansas	California	Colorado	Connecticut	Delaware	District of Columbia	Florida	Georgia	Hawaii	Idaho	Illinois	Indiana	Iowa	Kansas	Kentucky	Louisiana	Maine	Maryland
	ALABAMA																					
1	Medical College of Alabama, Birmingham	1	..	..	..	4	..	1	..	1	..	..	..	..	..	1	..	..	..	4	..	..
	ARKANSAS																					
2	University of Arkansas School of Medicine, Little Rock	3	1	..	..	10	1	1	..	1	..	1	..	..	3	..	..	2	..	8	..	1
	CALIFORNIA																					
3	College of Medical Evangelists, Loma Linda, Los Angeles	..	1	3	1	18	..	3	..	1	..	..	1	1	2	3	3	..	2	1	2	7
4	University of California School of Medicine, Los Angeles	..	..	..	..	..	1	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
5	University of Southern California School of Medicine, Los Angeles	..	..	..	..	12	..	..	..	..	..	..	1	1	..	..	..	..	..	1	..	..
6	Stanford University School of Medicine, Palo Alto	..	..	3	..	19	1	2	..	1	..	..	..	..	..	1	..	1	..	..	..	1
7	University of California School of Medicine, San Francisco	..	..	..	..	1	..	1	..	..	..	..	..	..	..	..	..	..	1	1	..	1
	COLORADO																					
8	University of Colorado School of Medicine, Denver	..	..	8	..	23	1	..	..	1	..	..	..	1	..	1	..	1	1	1	1	2
	CONNECTICUT																					
9	Yale University School of Medicine, New Haven	3	..	..	..	18	1	31	..	..	..	2	..	..	2	..	..	1	..	..	..	4
	DISTRICT OF COLUMBIA																					
10	Georgetown University School of Medicine, Washington	1	..	..	..	15	..	12	..	19	..	1	..	..	..	..	2	..	..	1	..	11
11	George Washington University School of Medicine, Washington	1	..	2	..	31	1	2	..	26	..	1	..	2	3	2	1	3	1	..	1	25
12	Howard University College of Medicine, Washington	..	..	..	..	22	..	1	..	14	..	1	..	..	..	1	..	..	..	1	..	2
	FLORIDA																					
13	University of Miami School of Medicine	..	..	..	..	6	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
	GEORGIA																					
14	Emory University School of Medicine, Emory University	4	..	..	1	6	..	..	..	..	..	..	..	..	1	2	..	..	1	5	..	1
15	Medical College of Georgia, Augusta	3	..	..	..	5	..	1	..	..	..	..	..	..	..	..	..	..	1	6	..	4
	ILLINOIS																					
16	Chicago Medical School	..	..	1	1	28	..	4	..	..	..	..	..	..	16	..	..	2	..	..	..	..
17	Northwestern University Medical School, Chicago	..	1	2	..	50	7	1	..	..	..	2	5	4	16	4	3	3	..	2	..	2
18	Stritch School of Medicine of Loyola University, Chicago	1	..	1	1	23	..	2	..	1	..	..	..	..	14	3	1	..	4	..	..	1
19	University of Chicago, The School of Medicine	..	1	1	1	25	1	3	..	5	..	1	2	..	16	4	..	3	..	..	..	4
20	University of Illinois College of Medicine, Chicago	1	..	4	1	79	4	..	..	1	..	..	2	..	16	15	3	1	..	1	..	2
	INDIANA																					
21	Indiana University School of Medicine, Indianapolis	..	1	3	..	40	3	1	1	..	..	1	..	..	6	1	2	3	4	1	..	3
	IOWA																					
22	State University of Iowa College of Medicine, Iowa City	..	2	9	..	53	2	..	..	..	..	..	..	1	3	2	1	1	..	2	..	2
	KANSAS																					
23	University of Kansas School of Medicine, Lawrence, Kansas City	..	..	5	3	34	3	1	..	..	..	..	1	3	2	1	1	2	1	1	..	1
	KENTUCKY																					
24	University of Louisville School of Medicine	1	..	..	..	14	..	2	..	1	..	1	..	..	3	17	1	..	..	2	..	..
	LOUISIANA																					
25	*Louisiana State University School of Medicine, New Orleans*	..	..	..	1	10	..	..	..	..	..	2	..	..	..	1	2	1	1	2	..	..
26	Tulane University School of Medicine, New Orleans	14	..	4	3	28	1	1	..	..	..	6	..	2	..	1	1	..	3	10	1	1
	MARYLAND																					
27	Johns Hopkins University School of Medicine, Baltimore	..	1	1	..	24	2	3	..	3	..	2	..	..	3	4	1	..	1	..	..	1
28	University of Maryland School of Medicine & College of Physicians and Surgeons, Baltimore	..	1	1	..	20	1	3	1	5	..	1	..	1	2	1	1	..	..	2	..	2
	MASSACHUSETTS																					
29	Boston University School of Medicine	..	1	1	..	25	1	3	..	1	..	..	1	..	1	..	..	..	1	..	2	1
30	Harvard Medical School, Boston	2	..	1	..	37	..	9	1	4	..	2	2	3	4	..	..	2	2	1	3	3
31	Tufts University School of Medicine, Boston	..	..	..	..	24	..	15	..	5	..	1	..	..	4	2	..	2	..	..	4	2
	MICHIGAN																					
32	University of Michigan Medical School, Ann Arbor	..	..	6	..	57	4	1	..	1	..	2	1	..	4	7	3	..	..	5	2	3
33	Wayne State University College of Medicine, Detroit	..	..	2	..	22	2	1	..	..	..	1	..	..	1	..	..	..	3	..	..	..
	MINNESOTA																					
34	University of Minnesota Medical School, Minneapolis	..	2	4	1	43	4	2	..	1	..	..	..	2	..	2	3	..	..	..	..	..
	MISSISSIPPI																					
35	University of Mississippi School of Medicine, Jackson	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	3	..	..
	MISSOURI																					
36	University of Missouri School of Medicine, Columbia	..	..	..	..	2	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
37	Saint Louis University School of Medicine	..	..	2	..	41	5	3	1	..	..	1	1	2	2	5	1	..	3	3	..	1
38	Washington University School of Medicine, St. Louis	1	..	1	2	38	5	3	..	..	..	1	..	1	3	4	2	2	1	..	..	4
	NEBRASKA																					
39	Creighton University School of Medicine, Omaha	..	..	3	..	23	5	..	..	..	..	..	2	..	3	2	8	..	1	1	..	1
40	University of Nebraska College of Medicine, Omaha	..	..	7	..	26	8	..	..	..	..	..	..	1	3	6	5	5	..	2	..	1
	NEW YORK																					
41	Albany Medical College of Union University	..	..	..	..	17	2	5	..	1	..	..	..	..	2	..	1	1	..	..	..	1
42	University of Buffalo School of Medicine	1	..	4	..	22	..	1	..	2	..	..	1	..	2	..	..	1	1	1	..	..
43	Albert Einstein College of Medicine of Yeshiva University, New York City	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
44	Columbia University College of Physicians and Surgeons, New York City	..	..	1	..	33	1	14	..	2	..	..	1	..	3	..	1	..	..	..	4	5
45	Cornell University Medical College, New York City	..	1	1	..	19	1	6	..	3	..	1	..	..	2	1	..	..	1	..	2	1
	Marginal Numbers	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21

22 Massachusetts	23 Michigan	24 Minnesota	25 Mississippi	26 Missouri	27 Montana	28 Nebraska	29 Nevada	30 New Hampshire	31 New Jersey	32 New Mexico	33 New York	34 North Carolina	35 North Dakota	36 Ohio	37 Oklahoma	38 Oregon	39 Pennsylvania	40 Rhode Island	41 South Carolina	42 South Dakota	43 Tennessee	44 Texas	45 Utah	46 Vermont	47 Virginia	48 Washington	49 West Virginia	50 Wisconsin	51 Wyoming	52 Canal Zone, Guam, Puerto Rico, and Virgin Islands	53 Totals	Marginal Numbers
1	1	..	..	..	..	..	..	..	..	..	..	2	..	..	..	..	..	..	..	..	..	1	..	..	1	..	..	..	..	..	18	1
1	6	3	..	5	..	..	..	..	..	1	..	1	..	2	3	..	..	..	..	..	1	19	1	..	..	1	3	..	..	..	79	2
5	..	3	1	2	2	..	2	..	..	..	4	4	..	4	1	6	3	..	1	..	8	5	1	..	1	3	..	..	1	2	108	3
..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	1	4
..	..	2	..	..	..	..	1	..	1	1	2	..	1	..	..	..	..	..	..	1	..	1	..	..	..	..	..	..	..	..	25	5
1	1	4	..	2	..	1	2	..	..	..	4	..	1	1	..	1	..	..	..	..	..	..	2	..	..	2	..	..	..	..	51	6
4	1	..	..	1	..	..	..	..	..	1	2	..	..	2	..	..	..	..	..	1	..	..	2	..	1	2	..	..	..	..	22	7
..	4	1	..	2	1	2	1	..	1	7	4	..	..	1	..	3	2	..	1	1	..	3	1	..	..	1	..	1	2	..	80	8
11	1	3	1	2	..	..	..	1	5	..	26	2	..	4	..	..	4	..	1	..	..	2	2	..	..	1	..	1	..	..	129	9
15	..	1	..	..	..	..	..	..	10	1	37	1	1	3	..	..	9	3	1	..	1	..	..	..	12	..	..	1	..	..	159	10
2	..	1	1	1	..	..	1	..	4	2	14	..	..	6	1	2	10	..	..	1	2	3	7	..	17	1	1	3	..	1	183	11
..	5	..	..	2	..	..	..	..	5	..	10	1	1	4	..	..	3	..	..	..	..	3	..	..	1	..	..	..	..	..	77	12
..	..	..	..	..	..	..	..	..	..	..	..	..	..	1	..	1	..	..	..	..	..	..	..	..	..	..	1	..	..	..	9	13
..	..	..	..	1	..	..	..	..	1	..	2	4	..	..	..	..	2	..	3	..	5	2	..	..	1	..	..	..	..	..	42	14
..	..	..	1	1	..	..	..	..	..	..	..	1	..	..	1	..	..	..	2	..	2	2	..	..	1	..	..	..	..	..	31	15
2	1	1	..	1	..	..	..	..	7	..	41	..	..	..	..	..	6	..	..	..	..	..	..	..	..	..	..	..	..	..	111	16
4	5	11	1	3	4	3	..	..	1	6	9	2	..	9	2	4	7	..	3	2	..	7	1	..	..	4	2	10	..	..	203	17
1	2	2	..	1	..	..	1	..	3	..	5	..	..	4	..	2	3	..	..	..	..	2	..	..	2	..	..	3	..	..	83	18
5	4	2	..	2	..	..	1	..	4	..	14	2	..	3	1	2	3	..	..	..	1	1	..	..	1	3	1	3	..	..	120	19
..	6	7	1	8	..	..	1	..	..	..	7	1	..	6	1	..	2	..	..	3	..	6	1	..	1	3	1	9	..	..	221	20
3	13	6	..	..	1	1	..	1	..	2	7	..	..	12	1	1	2	..	..	..	1	..	1	..	1	1	1	2	..	..	127	21
..	11	10	..	2	1	1	1	..	2	..	3	..	..	6	1	4	1	..	..	2	..	8	1	..	1	6	2	4	..	..	140	22
2	..	1	..	26	1	..	1	..	2	4	2	1	..	1	3	4	..	..	..	1	..	4	1	..	..	3	2	1	..	..	119	23
2	3	1	..	..	..	..	..	..	2	1	4	..	..	6	..	1	1	..	..	..	5	4	..	..	1	..	..	..	..	..	73	24
..	1	1	2	1	..	..	..	..	..	..	1	1	..	..	..	1	..	..	..	..	2	8	..	..	3	..	..	..	2	..	43	25
4	..	1	4	..	1	3	1	..	6	1	5	1	..	3	..	1	3	..	1	1	5	11	1	..	..	..	3	2	1	..	135	26
12	2	2	..	1	..	..	..	..	7	..	19	4	1	4	1	2	3	..	..	..	2	1	3	..	4	..	..	1	..	..	115	27
5	6	3	..	1	..	..	..	..	4	1	9	3	..	5	2	1	10	1	2	..	1	1	1	..	5	1	4	..	1	..	109	28
43	..	..	1	..	..	..	..	1	3	..	22	..	..	3	1	..	4	2	..	..	..	..	..	2	1	1	..	..	..	..	122	29
64	6	6	3	2	1	..	..	6	6	1	31	..	2	10	..	4	6	3	2	..	1	..	..	2	3	6	3	..	..	2	246	30
63	..	1	..	2	..	..	..	4	1	..	19	1	..	7	..	..	3	11	..	..	..	1	..	..	2	2	1	1	..	..	178	31
..	4	5	1	1	..	..	..	..	3	2	9	..	..	10	..	6	3	..	..	1	2	7	1	1	..	3	..	1	..	..	156	32
..	..	3	..	..	..	..	1	..	..	..	6	..	..	2	..	..	2	..	..	..	..	..	..	..	2	2	..	..	..	..	50	33
1	2	..	..	3	3	..	1	..	1	2	8	..	1	2	3	7	3	..	..	2	..	3	1	..	..	5	..	8	1	..	121	34
..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	1	..	..	..	..	..	..	..	..	4	35
..	..	1	..	..	1	..	..	..	..	1	..	..	..	..	..	..	..	..	..	..	..	2	..	..	..	..	..	..	..	..	7	36
3	6	9	..	..	1	..	..	..	1	3	6	1	..	12	2	1	4	..	..	..	1	4	..	..	2	3	1	3	..	..	134	37
4	1	2	..	2	2	..	..	..	3	1	5	..	..	3	5	1	2	..	..	..	3	3	..	..	1	1	3	4	1	..	115	38
3	..	7	1	1	2	2	2	..	..	1	6	..	1	..	..	2	1	..	..	3	..	4	..	..	..	..	..	1	1	1	88	39
..	..	5	..	6	2	..	..	..	1	2	3	1	..	2	1	2	2	..	1	1	..	2	1	..	..	11	1	4	1	..	113	40
4	..	4	..	..	1	..	..	..	3	..	43	..	..	1	..	..	4	1	..	..	..	..	..	1	1	..	1	1	..	..	95	41
4	..	3	..	..	..	..	1	..	3	..	62	..	..	7	..	..	3	..	..	..	..	2	1	1	..	2	..	..	..	1	126	42
..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	...	43
15	4	5	..	4	3	..	..	3	22	..	82	1	1	5	1	..	8	1	2	..	..	..	1	..	7	1	..	1	..	..	252	44
8	1	..	..	..	..	..	..	3	12	..	50	..	..	4	..	1	1	1	1	..	4	1	1	1	2	..	1	..	1	..	132	45
22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40	41	42	43	44	45	46	47	48	49	50	51	52	53	

TABLE 10.—*Candidates Licensed by Reciprocity and*

Marginal Number	School	Alabama	Alaska	Arizona	Arkansas	California	Colorado	Connecticut	Delaware	District of Columbia	Florida	Georgia	Hawaii	Idaho	Illinois	Indiana	Iowa	Kansas	Kentucky	Louisiana	Maine	Maryland
	Marginal Numbers	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
	New York—continued																					
46	New York Medical College, Flower & Fifth Avenue Hospitals, New York City	1	..	..	..	31	1	20	..	..	..	..	3	1	..	..	..	..	..	..	..	1
47	New York University College of Medicine, New York City	..	..	1	..	48	1	13	..	4	..	..	..	..	2	..	..	..	2	..	..	1
48	State University of New York, Downstate Medical Center, New York City	..	1	..	..	49	..	10	..	2	..	..	..	..	..	..	..	1	2	..	..	2
49	University of Rochester School of Medicine and Dentistry	..	1	..	..	19	2	2	..	3	..	1	1	..	..	..	..	1	3	..	1	1
50	State University of New York, Upstate Medical Center, Syracuse	..	..	1	..	17	1	7	..	2	..	..	..	..	3	..	..	1	..	..	..	3
	NORTH CAROLINA																					
51	University of North Carolina School of Medicine, Chapel Hill	..	..	..	..	4	..	..	..	1	..	2	..	..	..	1	..	..	..	..	..	..
52	Duke University School of Medicine, Durham	2	..	1	..	15	..	2	..	..	..	3	..	..	1	2	..	..	1	4	..	..
53	Bowman Gray School of Medicine of Wake Forest College, Winston-Salem	1	..	..	..	4	1	..	..	1	..	6	..	..	..	..	1	1	1	..	..	1
	OHIO																					
54	University of Cincinnati College of Medicine	1	..	2	..	33	2	1	..	2	..	1	..	..	4	7	..	..	2	1	..	2
55	Western Reserve University School of Medicine, Cleveland	..	..	1	..	30	4	..	..	..	..	1	..	1	1	4	2	..	..	..	1	1
56	Ohio State University College of Medicine, Columbus	1	1	2	..	32	6	..	..	3	..	..	..	..	4	8	1	3	1	..	..	1
	OKLAHOMA																					
57	University of Oklahoma School of Medicine, Oklahoma City	..	..	1	1	15	5	..	..	1	..	..	..	1	2	..	..	2	1	4	..	2
	OREGON																					
58	University of Oregon Medical School, Portland	..	..	3	..	25	..	..	..	..	..	..	..	4	..	..	..	..	1	..	..	..
	PENNSYLVANIA																					
59	Hahnemann Medical College and Hospital of Philadelphia	1	..	..	..	12	1	5	3	1	..	..	..	1	1	2	1	..	..	1	2	3
60	Jefferson Medical College of Philadelphia	1	..	2	..	28	4	4	1	3	..	1	..	1	4	2	3	..	1	1	..	6
61	Temple University School of Medicine, Philadelphia	..	..	..	..	13	3	3	2	1	..	2	..	..	4	1	1	..	2	1	..	3
62	University of Pennsylvania School of Medicine, Philadelphia	..	2	..	..	28	1	7	3	1	..	1	..	1	..	1	2	1	4	2	3	1
63	Woman's Medical College of Pennsylvania, Philadelphia	2	..	..	..	13	..	2	..	..	..	1	..	..	1	2	..	1	3	..	..	1
64	University of Pittsburgh School of Medicine	..	..	..	..	14	..	1	..	..	..	..	..	1	1	5	2	..	1	..	..	2
	PUERTO RICO																					
65	University of Puerto Rico School of Medicine, San Juan	..	..	..	..	4	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	1
	SOUTH CAROLINA																					
66	Medical College of South Carolina, Charleston	..	..	1	1	7	1	..	..	..	..	9	..	..	..	2	..	..	1	2	..	..
	TENNESSEE																					
67	University of Tennessee College of Medicine, Memphis	11	..	3	5	19	2	..	..	1	..	14	..	1	1	4	..	1	19	6	..	1
68	Meharry Medical College, Nashville	3	..	..	..	26	..	..	..	1	..	..	..	..	..	2	1	..	..	3	..	1
69	Vanderbilt University School of Medicine, Nashville	5	..	1	1	6	1	1	..	1	..	4	..	..	..	3	2	..	1	3	..	..
	TEXAS																					
70	University of Texas Southwestern Medical School, Dallas	..	1	..	..	13	1	1	..	..	..	..	..	..	..	1	..	..	..	10	..	1
71	University of Texas Medical Branch, Galveston	..	..	3	3	16	4	..	..	..	..	..	..	..	1	2	..	2	..	..	1	2
72	Baylor University College of Medicine, Houston	2	..	1	1	10	3	..	..	..	..	1	..	..	..	1	..	1	1	2	..	2
	UTAH																					
73	University of Utah School of Medicine, Salt Lake City	..	..	2	..	12	1	1	..	1	..	..	1	1	..	..	..	..	..	..	..	..
	VERMONT																					
74	University of Vermont College of Medicine, Burlington	..	..	..	..	10	2	7	..	2	..	1	..	..	1	..	2	..	1	..	1	4
	VIRGINIA																					
75	University of Virginia School of Medicine, Charlottesville	2	..	..	..	10	..	1	..	1	..	..	..	..	..	1	1	..	1	..	..	4
76	Medical College of Virginia, Richmond	..	..	3	..	2	..	..	1	1	..	1	..	..	1	1	..	1	2	5	..	3
	WASHINGTON																					
77	University of Washington School of Medicine, Seattle	..	..	..	..	17	1	1	..	..	..	..	..	2	..	..	1	..	1	..	..	..
	WISCONSIN																					
78	University of Wisconsin Medical School, Madison	..	..	5	..	22	3	..	..	..	..	..	..	..	6	1	3	2	1	1	..	..
79	Marquette University School of Medicine, Milwaukee	..	..	2	1	19	1	1	..	..	..	1	..	..	5	2	1	1	..	..	..	4
	CANADA																					
80	University of Alberta Faculty of Medicine, Edmonton	..	..	..	..	3	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
81	[illegible] edicine,	..	..	..	..	3	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
82	University of Manitoba Faculty of Medicine, Winnipeg	..	..	..	..	13	..	1	..	..	..	..	..	..	..	1	..	..	..	..	..	..
83	Dalhousie University Faculty of Medicine, Halifax	..	..	..	..	1	..	..	..	..	..	..	..	..	..	1	..	..	..	..	..	..
84	Queen's University Faculty of Medicine, Kingston	..	..	..	..	2	..	..	..	..	..	1	..	..	..	..	..	..	..	..	..	..
85	University of Western Ontario Faculty of Medicine, London	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	2	..	..	..	..	..
86	University of Ottawa Faculty of Medicine, Ottawa	..	..	..	..	2	..	..	..	..	..	1	..	..	1	..	..	..	..	..	..	..
87	University of Toronto Faculty of Medicine, Toronto	..	..	..	..	6	..	..	..	2	..	..	..	..	1	..	..	..	..	..	..	..
88	McGill University Faculty of Medicine, Montreal	..	..	..	..	18	2	4	..	..	..	..	..	..	2	3	..	..	1	..	3	2
89	University of Montreal Faculty of Medicine, Montreal	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	1	..	..	..
90	Laval University Faculty of Medicine, Quebec	..	..	..	..	1	..	..	..	..	..	..	..	..	..	..	1	..	..	..	..	..
91	[illegible]	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
	OTHERS																					
92	Foreign Medical Faculties	2	..	..	..	..	..	4	..	32	..	8	..	..	..	28	9	..	1	..	10	..
93	Extinct Medical Schools	..	..	2	..	6	..	1	..	..	..	..	..	..	..	1	2	..	..	..	..	..
94	Unapproved Medical Schools	..	..	..	..	7	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
95	Schools of Osteopathy	..	..	..	..	..	4	..	1	..	..	..	..	..	..	11	..	7	..	..	..	..
	Totals	72	19	121	29	1,732	126	239	15	167	..	91	26	40	219	197	85	63	90	114	44	157
	Marginal Numbers	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21

22 Massachusetts	23 Michigan	24 Minnesota	25 Mississippi	26 Missouri	27 Montana	28 Nebraska	29 Nevada	30 New Hampshire	31 New Jersey	32 New Mexico	33 New York	34 North Carolina	35 North Dakota	36 Ohio	37 Oklahoma	38 Oregon	39 Pennsylvania	40 Rhode Island	41 South Carolina	42 South Dakota	43 Tennessee	44 Texas	45 Utah	46 Vermont	47 Virginia	48 Washington	49 West Virginia	50 Wisconsin	51 Wyoming	52 Canal Zone, Guam, Puerto Rico, and Virgin Islands	53 Totals	Marginal Numbers
10	1	8	..	2	..	..	1	3	27	1	71	..	..	2	..	..	11	3	1	..	..	..	1	..	1	1	..	1	..	1	204	46
9	2	..	..	..	1	..	1	..	21	..	109	..	..	6	..	1	4	..	..	..	..	1	..	1	6	3	..	1	..	1	239	47
8	1	2	..	..	..	..	..	..	27	1	132	..	..	3	..	..	6	3	..	..	..	3	..	..	1	1	2	..	..	1	258	48
6	2	2	..	2	1	..	..	1	2	1	35	1	..	5	..	..	2	..	..	..	1	..	1	..	1	5	1	1	1	..	106	49
3	..	..	..	..	..	..	1	..	..	..	44	..	..	3	..	..	5	..	1	..	..	1	..	..	..	..	..	..	..	..	93	50
..	..	..	..	1	..	..	..	..	..	..	1	..	..	..	..	..	..	..	1	..	..	1	..	..	1	..	..	..	..	..	13	51
1	..	1	..	1	..	..	..	..	1	..	5	1	..	1	..	..	2	..	2	..	1	1	..	..	5	..	..	..	..	..	53	52
3	..	..	..	1	..	..	..	1	1	..	6	..	..	1	..	..	2	..	2	..	1	1	..	..	..	..	..	..	..	..	36	53
1	5	2	..	2	..	..	..	..	3	..	1	..	..	1	..	3	1	..	..	..	2	3	2	..	2	1	3	..	..	..	90	54
5	4	1	..	2	..	1	..	..	3	1	10	..	..	2	..	1	3	..	..	1	1	2	..	..	..	1	1	2	..	..	90	55
..	11	1	..	..	1	..	..	..	1	1	1	1	..	..	1	..	5	..	2	..	1	3	..	..	1	..	3	7	..	..	103	56
1	..	2	..	2	1	..	..	..	..	4	1	..	..	1	1	..	2	..	..	..	..	7	..	..	..	..	..	..	..	..	57	57
..	..	3	..	..	..	..	1	..	1	..	..	..	..	1	..	18	..	..	..	..	1	..	2	..	..	4	..	..	1	1	66	58
4	1	3	..	2	..	..	..	..	18	..	13	..	..	6	..	..	7	1	..	..	1	..	..	..	..	..	2	..	..	..	92	59
3	4	3	..	..	1	..	1	1	20	2	12	1	1	4	..	1	14	1	2	..	1	3	1	..	3	..	1	..	..	1	143	60
5	3	5	..	1	2	..	2	1	21	..	18	1	1	3	..	1	6	..	..	..	..	2	1	..	3	2	1	..	..	1	116	61
8	4	2	..	1	1	..	..	..	11	2	13	2	..	6	1	..	32	..	2	..	..	..	3	2	4	..	2	5	..	1	160	62
1	..	..	..	..	1	..	..	..	2	1	7	..	..	3	..	..	5	..	1	..	1	1	..	..	..	1	..	..	..	..	50	63
1	1	2	..	1	..	1	1	..	3	..	5	2	..	6	..	1	5	..	..	..	2	2	..	..	2	..	4	..	..	1	67	64
..	..	..	..	..	..	..	..	..	..	..	1	..	..	..	..	..	1	..	..	..	..	..	..	..	..	..	..	..	..	12	22	65
..	..	..	1	1	..	..	..	..	1	..	..	5	..	1	..	..	3	..	1	..	..	..	2	..	4	..	4	..	..	..	47	66
1	3	..	7	4	..	..	1	..	2	3	10	1	..	1	3	1	2	..	2	..	25	10	1	..	6	3	4	..	..	..	178	67
..	5	..	..	3	..	..	..	..	3	..	5	4	..	8	2	..	2	..	..	..	3	5	..	..	..	1	..	..	..	..	75	68
2	2	2	2	..	..	..	..	..	..	..	5	..	..	1	1	..	..	..	..	..	..	4	..	..	1	..	2	..	..	..	51	69
..	..	..	..	1	2	..	1	..	..	..	..	1	..	1	2	..	..	..	..	..	..	1	..	..	1	1	..	..	1	..	40	70
..	2	3	..	3	1	..	..	..	..	7	1	1	..	1	..	1	2	..	..	..	..	1	2	..	..	3	..	..	..	..	62	71
1	5	2	..	..	..	..	1	..	..	..	2	2	1	1	3	..	2	1	..	..	..	..	..	..	..	2	1	1	..	..	53	72
..	1	..	..	..	..	1	1	..	..	1	1	..	..	1	..	2	..	..	..	..	..	..	19	..	..	4	..	..	..	..	50	73
13	..	..	..	..	..	..	..	3	1	1	20	..	..	2	..	..	1	..	1	..	..	1	..	2	..	1	..	1	1	..	79	74
1	5	1	..	..	..	..	..	..	2	..	9	5	1	1	..	..	..	..	1	..	2	3	..	..	..	1	4	..	..	..	57	75
..	1	4	1	2	1	..	..	..	2	..	4	6	..	10	..	..	6	..	..	1	3	8	..	..	7	2	7	..	..	1	57	76
..	1	..	..	..	2	..	..	..	..	..	2	..	1	1	..	1	..	..	..	..	..	..	1	..	..	17	..	1	..	..	50	77
3	2	3	..	1	..	1	..	..	..	..	4	1	..	3	1	1	2	..	..	1	1	5	..	..	1	4	..	4	..	..	82	78
3	10	4	..	1	..	..	..	..	1	..	3	..	..	5	1	3	3	..	..	1	..	3	..	..	..	1	..	4	1	..	82	79
..	..	..	..	..	1	..	..	..	..	..	..	..	..	..	..	1	..	..	..	1	..	..	1	..	..	1	..	..	..	..	8	80
..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	3	81
..	..	..	..	..	..	..	..	..	..	..	2	..	..	..	..	..	..	..	..	..	..	..	..	..	1	2	..	1	..	..	21	82
..	1	..	..	..	..	..	1	..	..	..	3	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	1	..	..	..	8	83
2	1	..	..	..	..	..	..	..	..	..	1	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	7	84
..	..	..	..	..	..	..	..	..	..	..	3	..	..	..	..	..	..	..	..	..	..	..	..	..	..	1	..	..	..	..	6	85
..	..	..	..	..	..	..	..	1	..	..	1	..	..	1	..	..	..	..	..	..	..	..	..	..	..	1	..	..	..	..	8	86
2	..	1	2	..	..	1	..	..	1	..	4	..	..	..	..	..	..	..	..	..	1	..	..	..	..	3	..	..	..	..	24	87
6	..	3	..	..	1	..	1	1	3	1	9	1	1	5	..	..	..	..	1	..	..	1	..	1	1	2	1	1	..	..	75	88
..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	1	89
1	..	..	..	..	..	..	..	..	..	..	1	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	4	90
..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	...	91
..	13	..	..	..	1	1	..	5	22	..	5	2	..	94	2	..	..	..	..	2	5	7	..	..	..	24	..	12	..	..	289	92
..	..	..	..	1	1	1	..	..	2	..	2	2	..	..	..	..	..	..	1	..	..	2	2	..	..	1	..	..	..	..	27	93
..	1	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	2	..	..	1	..	..	..	..	1	12	94
4	..	..	..	..	..	..	..	..	60	..	1	..	..	14	..	..	..	..	..	..	..	42	..	..	..	..	..	5	..	..	152	95
400	189	177	31	121	46	20	32	36	386	71	1,169	75	16	300	49	96	256	32	42	27	100	245	71	14	128	163	77	112	17	20	8,234	
22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40	41	42	43	44	45	46	47	48	49	50	51	52	53	

1943, as the result of the accelerated medical school curriculum and the efforts made to maintain civilian care during World War II at as high a level as possible while still providing for the needs of the military. In 1943, more physicians were registered than in any previous year. In the succeeding two years, the total figure declined; however, in 1946, there were 6,696 more registered than in 1943. A large number of medical officers were separated from service; this fact together with their subsequent licensure by endorsement of credentials indicating their return to private practice in states other than those in which they were licensed account, in large part, for this increase. The increase was also

TABLE 11.—*Licentiates Representing Additions to the Medical Profession, 1599*

	Examinations	Reciprocity and Endorsement	Total
Alabama	134	2	136
Alaska	0	2	2
Arizona	12	0	12
Arkansas	71	0	71
California	466	210	676
Canal Zone	0	1	1
Colorado	48	15	63
Connecticut	129	81	210
District of Columbia	8	45	53
Florida	143	0	143
Georgia	251	0	251
Hawaii	10	12	22
Idaho	1	3	4
Illinois	446	75	521
Indiana	166	1	167
Iowa	111	4	115
Kansas	54	6	60
Kentucky	93	6	99
Louisiana	220	0	220
Maine	24	8	32
Maryland	236	17	253
Massachusetts	32	195	227
Michigan	306	1	307
Minnesota	169	26	195
Mississippi	104	2	106
Missouri	271	10	281
Montana	3	1	4
Nebraska	120	1	121
New Hampshire	3	2	5
New Jersey	136	42	178
New Mexico	2	0	2
New York	337	784	1,121
North Carolina	192	0	192
North Dakota	12	0	12
Ohio	395	46	441
Oklahoma	78	6	84
Oregon	29	9	38
Pennsylvania	466	64	530
Puerto Rico	121	12	133
Rhode Island	25	19	44
South Carolina	93	3	96
South Dakota	11	0	11
Tennessee	193	3	196
Texas	319	0	319
Utah	4	18	22
Vermont	12	3	15
Virginia	244	8	252
Virgin Islands	1	0	1
Washington	61	27	88
West Virginia	23	1	24
Wisconsin	103	8	111
Wyoming	2	0	2
Totals	6,490	1,779	8,269

TABLE 12.—*Licentiates Representing Additions to the Medical Profession Grouped in Geographical Divisions, 1959*

	Examination	Reciprocity and Endorsement	Total
New England			
Maine	24	8	32
New Hampshire	3	2	5
Vermont	12	3	15
Massachusetts	32	195	227
Rhode Island	25	19	44
Connecticut	129	81	210
Totals	225	308	533
Middle Atlantic			
New York	337	784	1,121
New Jersey	136	42	178
Pennsylvania	466	64	530
Totals	939	890	1,829
East North Central			
Ohio	395	46	441
Indiana	166	1	167
Illinois	446	75	521
Michigan	306	1	307
Wisconsin	103	8	111
Totals	1,416	131	1,547
West North Central			
Minnesota	169	26	195
Iowa	111	4	115
Missouri	271	10	281
North Dakota	12	..	12
South Dakota	11	..	11
Nebraska	120	1	121
Kansas	54	6	60
Totals	748	47	795
South Atlantic			
Delaware	..	..	..
Maryland	236	17	253
District of Columbia	8	45	53
Virginia	244	8	252
West Virginia	23	1	24
North Carolina	192	..	192
South Carolina	93	3	96
Georgia	251	..	251
Florida	143	..	143
Totals	1,190	74	1,264
East South Central			
Kentucky	93	6	99
Tennessee	193	3	196
Alabama	134	2	136
Mississippi	104	2	106
Totals	524	13	537
West South Central			
Arkansas	71	..	71
Louisiana	220	..	220
Oklahoma	78	6	84
Texas	319	..	319
Totals	688	6	694
Mountain			
Montana	3	1	4
Idaho	1	3	4
Wyoming	2	..	2
Colorado	48	15	63
New Mexico	2	..	2
Arizona	12	..	12
Utah	4	18	22
Nevada	..	..	..
Totals	72	37	109
Pacific			
Alaska	..	2	2
Washington	61	27	88
Oregon	29	9	38
Hawaii	10	12	22
California	466	210	676
Totals	566	260	826
Possessions			
Canal Zone	..	1	1
Puerto Rico	121	12	133
Virgin Islands	1	..	1
Totals	122	13	135
Totals	6,490	1,779	8,269

occasioned by the licensure of recent graduates who had entered military service on completion of the internship and before securing state licensure.

In 1904, the first year shown, the percentage of failures was 19.3. This was an era of proprietary medical schools. Beginning in 1913, the percentage of failures gradually dropped each year, until 1930 when only 5.7% failed. Beginning in 1936, the percentage of failures began to rise, reaching another peak of 20.7% in 1940. This was the result of the increase in the number of foreign-trained physicians seeking licensure in the United States; many are *not* successful until after repeated attempts at licensure examinations. Since 1942, the percentage of failures has been somewhat reduced, although it still reflects the unsuccessful attempts of foreign-trained physicians, graduates of unapproved medical schools, and others.

TABLE 13.—*Licentiates Representing Additions to the Medical Profession, 1935-1959*

Year	Examination	Reciprocity and Endorsement	Total
1935	5,099	411	5,510
1936	5,548	629	6,177
1937	5,812	612	6,424
1938	5,759	501	6,260
1939	5,584	460	6,044
1940	5,432	455	5,887
1941	5,241	474	5,715
1942	5,560	454	6,014
1943	5,586	372	5,958
1944	6,495	470	6,695
1945	4,979	769	5,748
1946	5,362	1,608	6,970
1947	5,273	1,617	6,890
1948	4,942	1,694	6,636
1949	4,260	1,616	5,876
1950	4,609	1,393	6,002
1951	4,985	1,288	6,273
1952	5,168	1,717	6,885
1953	5,388	1,888	7,276
1954	5,897	2,020	7,917
1955	6,211	1,526	7,737
1956	6,035	1,428	7,463
1957	5,872	1,583	7,455
1958	6,155	1,654	7,809
1959	6,490	1,779	8,269
Totals	137,742	28,418	166,160

This table again refers to examinations given annually, rather than to individuals examined. A candidate who fails more than once in a state in a given year is counted as one failure; if he should again fail in a succeeding year, this fact is computed among the failures for that year. Likewise, a successful candidate securing a license in more than one state in a given year is counted in both states and is likewise counted if he passed at examinations in later years. Therefore, the figures in this table give only a fair approximation of the number of physicians added to the profession.

The number of physicians registered in 1959 was 16,068—the greatest number in 56 years. The number so registered after written examination was 7,834, whereas the number registered by reciprocity or endorsement of credentials was 8,234.

Graduates of Approved Schools and Others Registered, 1922-1959

Table 15 reflects for two categories the number of physicians registered since 1922. Prior to 1928, medical schools were classified by the Council on Medical Education and Hospitals of the American Medical Association as A, B, and C; for purposes of this table, the schools are arranged in two groups. The figures in the first group include graduates of medical schools rated in class A and B prior to 1928 and schools classified as approved institutions since 1928. The second group refers to class C graduates, graduates of medical schools classified as unap-

TABLE 14.—*Registration of Physicians, 1904-1959*

Year	Examined	Passed	% Failed	Reciprocity or Endorsement	Total Registered
1904	7,056	5,693	19.3	1,005	6,698
1905	7,178	5,688	20.8	394	6,082
1906	8,040	6,373	20.7	1,502	7,875
1907	7,279	5,731	21.3	1,427	7,158
1908	7,775	6,089	21.7	1,284	7,373
1909	7,295	5,865	19.6	1,381	7,246
1910	7,011	5,719	18.4	1,640	7,359
1911	6,964	5,582	19.8	1,243	6,825
1912	6,880	5,467	20.5	1,273	6,740
1913	6,453	5,253	18.6	1,292	6,545
1914	5,579	4,379	21.5	1,439	5,818
1915	5,334	4,507	15.5	1,399	5,906
1916	4,878	4,151	14.9	1,353	5,504
1917	4,754	4,085	14.0	1,360	5,445
1918	3,667	3,184	13.2	1,047	4,231
1919	4,750	4,074	14.2	2,546	6,620
1920	4,796	4,062	15.3	2,558	6,620
1921	4,825	4,228	12.4	2,186	6,414
1922	4,031	3,539	12.2	2,073	5,612
1923	4,727	4,028	14.8	2,405	6,433
1924	5,392	4,756	11.8	1,923	6,679
1925	6,002	5,450	9.2	1,861	7,311
1926	5,770	5,314	7.9	1,955	7,269
1927	5,389	5,002	7.2	2,176	7,178
1928	5,458	5,090	6.7	2,228	7,318
1929	5,629	5,252	6.2	2,420	7,702
1930	5,571	5,255	5.7	2,366	7,621
1931	5,611	5,263	6.2	2,211	7,476
1932	5,675	5,247	7.6	1,886	7,133
1933	5,673	5,244	7.6	1,989	7,233
1934	6,145	6,628	8.4	2,161	7,789
1935	6,443	5,859	9.1	2,194	8,053
1936	6,918	6,224	10.0	2,773	8,997
1937	7,334	6,604	10.0	3,205	9,809
1938	7,461	6,589	11.7	2,956	9,545
1939	7,754	6,493	16.3	2,872	9,365
1940	7,926	6,291	20.7	2,866	9,157
1941	7,539	6,057	19.7	2,762	8,819
1942	7,223	6,120	15.4	2,469	8,589
1943	8,403	7,489	10.9	2,340	9,829
1944	6,817	6,011	11.8	2,596	8,607
1945	5,930	5,343	9.9	3,622	8,965
1946	7,610	6,856	9.9	9,669	16,525
1947	7,164	6,414	10.5	7,701	14,115
1948	6,624	5,904	10.8	7,595	13,499
1949	5,963	5,219	12.5	6,929	12,148
1950	6,203	5,481	11.6	6,755	12,236
1951	6,473	5,716	11.7	6,225	11,941
1952	7,028	6,229	11.3	7,016	13,245
1953	7,425	6,543	13.0	7,869	14,412
1954	8,066	7,033	12.7	8,202	15,235
1955	8,501	7,400	12.9	7,461	15,962
1956	8,342	7,179	13.9	7,421	14,600
1957	9,116	7,769	14.8	7,486	15,255
1958	8,633	7,268	15.8	7,925	15,193
1959	8,996	7,834	12.9	8,234	16,068

proved since 1928, graduates of foreign medical faculties, and graduates of schools of osteopathy given recognition by medical licensing boards. In 1928, the classification of medical schools in A, B and C groups was discontinued by the Council, and a list of approved medical schools has since been maintained. The current listing of approved medical schools in the United States and Canada appears annually in the Education Number of THE JOURNAL.[3]

In 1959, there were 16,068 candidates registered; 13,584 of these (84.5%) represented graduates of approved schools and 2,484 (15.5%) were in the second group. In the 38 years recorded in this table, 391,284 were registered, including 351,427 (89.7%) graduates of medical schools indicated as in the approved group and 40,397 others (10.2%).

TABLE 15.—*Graduates of Approved Schools and Others Registered, 1922-1959*

	Graduates of Approved Schools		Others		
Year	No.	Percentage of Total	No.	Percentage of Total	Totals
1922	4,519	80.5	1,093	19.5	5,612
1923	5,196	80.8	1,237	19.2	6,433
1924	5,687	85.1	992	14.9	6,679
1925	6,314	86.4	997	13.6	7,311
1926	6,441	88.7	828	11.3	7,269
1927	6,410	89.4	768	10.6	7,178
1928	6,585	90.1	733	9.9	7,318
1929	7,003	91.0	699	9.0	7,702
1930	7,011	92.1	610	7.9	7,621
1931	6,932	92.8	544	7.2	7,476
1932	6,676	92.1	457	6.3	7,133
1933	6,771	93.7	459	6.3	7,233
1934	7,172	92.1	617	7.9	7,789
1935	7,360	91.3	693	8.5	8,053
1936	7,931	88.1	1,063	11.8	8,997
1937	8,391	85.5	1,418	14.4	9,809
1938	8,315	87.1	1,230	12.9	9,545
1939	8,067	86.2	1,298	13.8	9,365
1940	7,781	85.0	1,376	15.0	9,157
1941	7,770	87.9	1,049	11.9	8,819
1942	7,290	84.9	1,299	15.1	8,589
1943	8,640	87.9	1,189	12.2	9,829
1944	7,737	89.8	870	10.1	8,607
1945	8,233	91.8	732	8.1	8,965
1946	15,692	94.9	835	5.1	16,527
1947	13,097	93.0	1,018	7.0	14,115
1948	12,791	94.8	708	5.2	13,499
1949	11,378	93.7	770	6.3	12,148
1950	11,502	94.0	734	6.0	12,236
1951	11,027	92.3	914	7.7	11,941
1952	12,198	92.1	1,047	7.9	13,245
1953	13,189	91.5	1,223	8.5	14,412
1954	13,814	90.7	1,421	9.3	15,235
1955	13,344	89.8	1,517	10.2	14,861
1956	13,146	90.0	1,454	10.0	14,600
1957	13,330	87.4	1,925	12.1	15,255
1958	13,097	86.2	2,096	13.8	15,193
1959	13,584	84.5	2,484	15.5	16,068
Totals	351,427	89.7	40,397	10.2	391,824

Graduates of Unapproved Medical Schools Registered, 1954-1959

Graduates of institutions that were classified by the Council on Medical Education and Hospitals of the American Medical Association as unapproved were registered in 26 states, the District of Columbia, and the territories and possession in the past six years. Figures are reported separately in table 16 for those licensed after written examination and those licensed by reciprocity or endorsement of credentials. The table also includes a column combining the figures for these two groups. In the main, they represent five schools more recently in operation. At present, there is no medical school in complete operation within the United States and Canada that is not approved by the Council on Medical Education and Hospitals.

There were 214 graduates of unapproved medical schools registered in the six-year period 1954-1959, 65 by examination and 149 by endorsement of credentials. In 1959, there were 9 licensed by five boards by examination and 12 by five boards by reciprocity or endorsement of credentials. California, Florida, New York, and Texas licensed the greatest number of graduates from unapproved medical schools during this six-year period. The remainder of the states shown registered fewer than 10.

Graduates of Schools of Osteopathy Registered by Medical Examining Boards, 1954-1959

The number of graduates of schools of osteopathy granted the privilege of practicing medicine, surgery, or both, by 18 medical examining boards for six years (1954-1959) is given in table 17. There have been 1,762 such persons registered—1,149 by examination in 15 states and 613, without written examination, by 16 boards. Following is a summary of the actions and regulations of the 18 boards providing for the licensing of osteopaths by the medical examining board.

In Colorado, an osteopath receives a license to practice medicine and must meet the same requirements as for doctors of medicine: namely, qualification in the basic sciences of anatomy, physiology, chemistry, bacteriology, and pathology; after December 31, 1935, two years of preprofessional education in a college acceptable to the board; and not less than four grades of resident courses of professional study of not less than nine months each.

In Connecticut, an osteopath registered by the osteopathic board may be licensed to practice medicine and surgery or both after examination by the medical examining board. Osteopaths in Delaware may be licensed as osteopathic physicians after successfully passing the examination of the medical board, except that the principles of osteopathy are given in the examination in place of materia medica and therapeutics.

The District of Columbia will permit any person engaged in the practice of osteopathy on or before Jan. 1, 1948, to file application for a license to practice osteopathy and surgery. To obtain such a license, an osteopath must pass all subjects of the medical examination with one exception—examination is given in the practice of osteopathy instead of the practice of medicine. Osteopaths are eligible for licensure by endorsement of the certificate issued by the National Board of Osteopathic Medical Examiners.

Since 1950, in Illinois, graduates of the Chicago College of Osteopathy are examined by the medical board and may receive medical licenses. In Indiana, under an amendment to the medical practice act in 1945, osteopaths are permitted to practice medicine, surgery, and obstetrics and to administer anesthetics, antiseptics, and narcotics. Persons who were licensed in osteopathy before 1945 may obtain from the medical board a license to practice osteopathy, surgery, and obstetrics.

TABLE 16.—*Graduates of Unapproved Medical Schools Registered 1954-1959*

	Examination							Reciprocity and Endorsement							Combined Totals
	1954	1955	1956	1957	1958	1959	Totals	1954	1955	1956	1957	1958	1959	Totals	
Arizona	..	..	..	..	..	..	..	1	..	..	1	..	..	2	2
Arkansas	..	..	..	..	..	..	..	..	..	..	2	1	..	3	3
California	..	..	..	..	..	..	..	19	15	2	5	11	7	59	59
Delaware	..	..	..	..	..	..	..	..	1	..	1	..	..	2	2
District of Columbia	..	..	..	..	..	..	..	..	..	1	1	1	..	3	3
Florida	8	7	4	5	1	1	26	..	..	..	..	..	..	..	26
Georgia	2	..	..	..	..	..	2	..	..	..	..	1	..	1	3
Idaho	..	..	..	..	..	..	..	..	..	..	1	..	..	1	1
Illinois	..	..	..	..	..	..	..	2	4	..	..	..	..	6	6
Iowa	..	..	..	..	..	..	..	1	1	..	..	..	..	2	2
Maine	..	1	..	..	..	..	1	..	1	..	..	..	..	1	2
Massachusetts	5	1	..	..	1	..	7	..	..	..	..	..	..	..	7
Michigan	..	..	..	..	..	..	..	1	..	1	1	1	1	5	5
Missouri	..	..	..	..	..	..	..	1	..	1	1	..	..	3	3
New Hampshire	..	..	..	..	..	..	..	..	..	1	..	..	..	1	1
New Jersey	1	..	..	..	..	..	1	..	..	4	1	..	..	5	6
New York	3	1	5	2	2	..	13	..	..	..	1	..	..	1	14
Ohio	..	3	..	..	..	..	3	3	..	..	..	..	..	3	6
Oregon	..	..	..	..	..	1	1	..	..	..	..	..	..	..	1
Pennsylvania	..	..	..	..	2	2	4	..	1	..	..	..	..	1	5
South Carolina	..	..	..	2	..	..	2	..	..	..	..	..	..	..	2
South Dakota	..	1	..	..	..	..	1	..	..	..	..	..	..	..	1
Tennessee	..	..	..	..	..	..	..	..	..	..	..	1	..	1	1
Texas	..	..	..	..	..	..	..	7	3	8	11	4	2	35	35
Virginia	..	..	..	..	..	..	..	..	..	..	..	..	1	1	1
Washington	..	..	..	..	..	..	..	..	..	..	1	2	..	3	3
Wisconsin	..	..	..	..	..	..	..	..	1	1	2	4	..	8	8
Territories and Possessions	2	..	..	..	..	2*	4	1	..	..	..	..	1†	2	6
Totals	21	14	9	9	6	6	65	36	27	19	29	26	12	149	214

* 1 each Canal Zone and Puerto Rico.
† Canal Zone.

A graduate from an approved college of osteopathy after June 1, 1950, who has served an internship and is the holder of a valid license to practice osteopathy in Kansas, may take the examination in medicine and surgery or may be endorsed from a composite state board.

In Massachusetts, for the purposes of registration, the D.O. degree is considered equivalent to the M.D. degree, and the applicants for licensure must meet the same requirements as those applicants for the M.D. degree. In New Hampshire, under the provisions of the medical practice act, osteopaths are granted the right to practice medicine and surgery.

The New Jersey medical practice act provides that an osteopath, licensed prior to Nov. 1, 1941, who has served for a period of two years as an intern or resident surgeon in an approved osteopathic or medical hospital, has completed a postgraduate course of two years in a college of osteopathy or medicine approved by the licensing board, or has had at least three years of practice in a hospital approved by the board, can be admitted to an examination in pharmacology, therapeutics, and surgery. If successful, he can obtain a license to practice medicine and surgery.

In New York, a licensed osteopath, who is an applicant for the right to use instruments for minor surgical procedures and to use anesthetics, antiseptics, narcotics, and biological products, may be granted the right to practice medicine, without limitation, if his credentials satisfy the Board of Regents. If not, such applicants shall be required either to pursue further study or to pass a special examination.

The Ohio Medical Practice Act provides that all graduates from osteopathic schools applying for the right to practice in the state must meet certain educational requirements and must pass certain examinations. One of the required examinations is in surgery. Those who qualify and pass all of the examinations are then given a license to practice osteopathic medicine and surgery. Those in practice and licensed under a more limited law in effect prior to 1943 can secure a license to practice osteopathic medicine and surgery by meeting certain additional requirements; these include postgraduate work and the successful completion of additional examinations.

In Oregon, osteopaths who meet certain requirements are granted the right to practice in the subjects covered by the medical examination, with the exception of the practice of medicine or materia medica and therapeutics. In South Dakota, graduates of approved schools of osteopathy may be licensed to practice medicine, surgery, and obstetrics. Texas issues only one license, which is unrestricted in scope.

In Virginia, two classes of osteopaths are licensed. If a candidate takes the same examination as an M.D., substituting the practice of osteopathy for the practice of medicine, he is licensed to practice osteopathy, with the use of surgery and drugs. If he takes an examination without the subjects of surgery and materia medica, he is licensed to practice osteopathy, without the use of drugs or surgery.

The Wisconsin law, amended in 1950, provides that an osteopath licensed in the state may obtain a license to practice medicine and surgery by completing a refresher course in materia medica and pharmacology consisting of not less than 64 hours of lecture and 60 hours of laboratory work and by passing an examination in these subjects. Osteopaths not licensed in the state may apply to take the same examination as physicians and, if successful, they will be granted licenses to practice medicine and surgery. In Wyoming, the statutes contain no specific provision for the licensing of osteopaths. The medical practice act provides that the certificate issued to all physicians shall be deemed a license to practice medicine in all brances in which the applicant has taken an examination.

TABLE 17.—*Graduates of Schools of Osteopathy Registered by Medical Boards, 1954-1959*

	Examination							Reciprocity and Endorsement							Combined Totals
	1954	1955	1956	1957	1958	1959	Totals	1954	1955	1956	1957	1958	1959	Totals	
Colorado	3	7	1	5	..	3	19	22	16	12	9	15	4	78	97
Connecticut	3	..	..	..	..	..	3	..	..	..	..	..	..	..	3
Delaware	..	2	3	1	..	1	7	1	2	1	1	9	1	15	22
District of Columbia	..	..	..	..	1	..	1	1	1	..	..	..	..	2	3
Illinois	..	14	10	2	6	8	40	..	..	11	..	..	..	11	51
Indiana	2	6	2	5	6	..	21	11	9	..	9	12	14	55	76
Kansas	..	.	..	144	16	2	162	..	..	..	..	4	7	11	173
Massachusetts	1	..	..	..	..	..	1	2	5	4	4	6	4	25	26
New Hampshire	..	..	..	1	1	..	2	1	3	1	2	1	..	8	10
New Jersey	7	8	6	9	2	2	34	18	7	28	10	45	60	168	202
New York	44	92	42	44	35	30	287	1	1	4	..	3	1	10	297
Ohio	81	73	63	66	66	101	450	13	2	13	10	3	14	55	505
Oregon	..	..	..	..	..	..	..	..	..	2	..	..	..	2	2
South Dakota	1	..	..	..	..	..	1	..	..	..	..	..	..	..	1
Texas	46	25	9	3	5	3	91	13	10	13	32	43	42	153	244
Virginia	..	..	..	..	..	..	..	1	..	..	..	..	..	1	1
Wisconsin	7	6	6	4	2	5	30	1	1	3	3	2	5	15	45
Wyoming	..	..	..	..	..	..	..	..	1	..	..	3	..	4	4
Totals	195	233	142	284	140	155	1,149	85	58	92	80	146	152	613	1,762

Enactment and Operation of Medical Practice Act

Table 18 records the year in which the first medical practice act was enacted in each state and the year in which the first board of medical examiners was established under the medical practice act. In some instances, the original act was repealed and a new law enacted. No attempt was made to indicate the amendments to the original medical practice act.

Preprofessional Training Requirements of Licensing Boards

Since January, 1953, the minimum requirement for admission to an approved medical school has been three years of college preparatory study. The Council on Medical Education and Hospitals, in accepting this minimum, recommends for most students a full four-year college course in order that a broader background education may be obtained. In its "Function and Structure of a Modern Medical School," published jointly by the Council and the Association of American Medical Colleges, provision is made for the unusually intelligent and mature student who may be admitted to medical school, under exceptional conditions, after two years of college work. Statements regarding minimal preprofessional collegiate requirements are presented in the brochure "Admission Requirements of American Medical Colleges" prepared by the Association of American Medical Colleges.

The majority of the medical practice acts have been amended to agree with the requirement of preprofessional education exacted by the Council and the Association of American Medical Colleges. This requirement is not specified in the laws of Arizona, Colorado, Iowa, Nevada, and Oklahoma, while the laws in Georgia and Missouri merely state that a high school diploma is a requirement. Two years of preprofessional college is the legal requirement in the Canal Zone, Delaware, District of Columbia, Illinois, Maryland, Massachusetts, Mississippi, New Jersey, New York, Ohio, Oregon, Rhode Island, Virginia, and West Virginia. The preprofessional requirement exacted by eight boards—California, Connecticut, Delaware, Massachusetts, New York, Puerto Rico, Washington, and Wisconsin—according to their medical practice acts, specify in detail the subjects which must be covered in preprofessional training.

Experiments in medical education, which are designed, in part at least, to break the barrier that has traditionally existed between colleges and schools of medicine, are being planned or have been implemented in several medical schools. These programs allow talented students at the end of the second or third college year to begin medical school studies while at the same time continuing liberal arts college courses.[4] The licensing boards, with a few exceptions, have indicated that students completing their medical training under one of the programs which are designed to shorten one year of formal education for selected students will be eligible for licensure as meeting the stated preprofessional requirements.

Approval of Medical Schools

Seven licensing boards maintain their own list of approved medical schools in the United States and Canada. Twenty-six boards require applicants for licensure from approved medical schools in the United States or Canada to be graduates of medical schools approved by the Council on Medical Education and Hospitals. Two boards require membership in the Association of American Medical Colleges. Twenty boards specify that schools must be approved by the Council and be in membership in the Association of American Medical Colleges. In 16 instances, the requirement is specified in the medical practice act; 37 boards reported that it is a formal regulation; 2 indicated that it was an informal policy. In actuality, all approved medical schools are both approved by the Council and in membership in the Association of American Medical Colleges.

Internship as a Prerequisite for Licensure

There is currently no medical school in the United States which requires that the student serve an internship as a prerequisite to graduation. Duke University School of Medicine specifies the internship requirement but does not withhold the degree until the internship is completed. The degree is issued at the end of the four-year medical course, but the school obtains from each student a signed agreement that he will spend two years in training in a hospital or laboratory before entering practice.

One year of internship, as a requirement for licensure, is required by 38 licensing boards. Seven boards specify that the internship must be a rotating service. Missouri requires the internship for reciprocity applicants only. Those licensing boards that require an internship as a prerequisite for licensure are listed in table 19. Specific requirements as to the content of the intern service or other regulation of the licensing board is indicated by footnote.

TABLE 18.—*Enactment and Operation of Medical Practice Act*

State	First Medical Practice Act Enacted	First Examining Board Established Under Medical Practice Act
Alabama	1877	1877
Alaska	..	..
Arizona	1913	1913
Arkansas	1909	1909
California	1876	1876
Canal Zone	1911	1933
Colorado	..	..
Connecticut	1875	1878
Delaware	1895	1895
District of Columbia	1896	1896
Florida	..	1921
Georgia	1913	..
Guam	1947	1947
Hawaii	..	..
Idaho	1893	1893
Illinois	1876	1876
Indiana	..	..
Iowa	1886	1886
Kansas	1901	1901
Kentucky	1874	1878
Louisiana	1894	1894
Maine	1895	1895
Maryland	1892	1892
Massachusetts	1894	1894
Michigan	1899	1899
Minnesota	1883	1883
Mississippi	1819	1819
Missouri	1903	1903
Montana	1889	1889
Nebraska	1881	1891
Nevada	1905	1905
New Hampshire	1915	1915
New Jersey	1890	1890
New Mexico	1901	1901
New York	1891	1891
North Carolina	1859	1859
North Dakota	1890	1890
Ohio	1896	1896
Oklahoma	1908	1908
Oregon	1889	1889
Pennsylvania	1911	1911
Puerto Rico	1905	1903
Rhode Island	1895	1895
South Carolina	1817	1900
South Dakota	1869	1885
Tennessee	1901	1901
Texas	1837	1907
Utah	1921	1921
Vermont	1904	1904
Virgin Islands	..	..
Virginia	..	..
Washington	1909	1909
West Virginia	1881	1881
Wisconsin	1897	1897
Wyoming	1899	1905

Temporary and Educational Permits, Limited and Temporary Licenses, or Other Certificates Issued by State Licensing Boards

Thirty-nine boards provide for the issuance of temporary and educational permits, limited and temporary licenses, or other certificates for the practice of medicine. The terms for the issuance of such certificates vary. This limited registration may apply to hospital training, to those ineligible for licensure who seek further educational training, or for regular practice until the next regular session of the licensing board. A list of these states and information on the length of validity of this special registration are shown in table 20.

TABLE 19.—*Medical Licensing Boards Requiring One-Year Internship*

Alabama
Alaska[1]
Arizona
California
Canal Zone[2]
Colorado
Delaware[3]
District of Columbia
Guam
Hawaii
Idaho
Illinois[4]
Iowa
Kansas
Kentucky
Louisiana[3]
Maine
Michigan
Missouri[5]
Montana
Nevada
New Hampshire
New Jersey[6]
North Dakota
Oklahoma
Oregon
Pennsylvania[7]
Puerto Rico[3]
Rhode Island[3]
South Carolina
South Dakota
Utah
Vermont
Virgin Islands
Washington[3]
West Virginia
Wisconsin
Wyoming

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1. After seven years from date of graduation from medical school, postgraduate training accepted in lieu of deficiencies in a rotating internship.
2. At the discretion of the board.
3. Internship must be a rotating service.
4. Rotating service must include at least three months each in Surgery, Medicine, and Obstetrics-Pediatrics; the remaining three months to be spent in either of these or medical specialties.
5. For reciprocity applicants.
6. One-year rotating service or two-year straight internship. At least three months of rotating service must be in general surgery; three months, general medicine; and six weeks, obstetrics.
7. Straight internship accepted after seven years from date of graduation from medical school. Internship must be a rotating service.

Licensure, Registration, or Other Requirements for Interns and Residents Serving in Hospitals

In the majority of states, physicians serving internships are not required to be licensed in the state in which the hospital where they are interning is located. Indiana and Puerto Rico have this requirement while Rhode Island and South Carolina will issue a temporary permit for internship training. The states which require some form of registration with the licensing board or a stipulation that the physician must be eligible for licensure are listed in table 21.

Thirty-two boards require that physicians serving as residents in hospitals must be licensed or stipulate registration in the state. Four boards indicate that registration must be in the form of a regular license. Other boards do not require full licensure of residents but issue certificates limited in nature, which may be called a limited license, a resident's license, temporary permit, or temporary license. In a few instances, a residency may be served for a specified period without licensure. The regulations of each of the licensing boards that exact some requirement of those engaged in residency training are given in table 22.

TABLE 20.—*Temporary and Educational Permits, Limited and Temporary Licenses, or Other Certificates Issued by State Licensing Boards*

Alaska	Temporary permits issued while processing permanent licensure, for physicians employed in the summer cannery season, and to physicians in the armed forces on short periods with private physicians, and for locum tenens work.
Arizona	Temporary permits issued on basis of community emergency.
Arkansas	Temporary permits issued in cases of emergency, valid until the next meeting of the board.
Connecticut	Educational permits granted to graduates of unapproved medical schools to serve in approved hospital training programs.
Delaware	Temporary emergency license granted for one year, subject to renewal, and for locum tenens practice.
District of Columbia	*Permit for federal physicians*; borderline permits for physicians licensed and practicing in contiguous counties of Maryland and Virginia to attend specific patients in the District of Columbia.
Georgia	Temporary permit until board meets. Institutional permit may be granted to physicians who are not citizens and/or foreign graduates.
Guam	Restrictive certificate to permit medical employees of federal contractors to practice in the discharge of their official duties.
Idaho	To candidates holding certificate of National Board of Medical Examiners or licensed by written examination in another state until next meeting of Board, to residents in hospitals, a temporary permit may be granted.
Illinois	Temporary certificate for residency training for applicants who are not qualified for permanent registration. Permit issued for service in state hospitals to physicians eligible for licensure.
Indiana	Temporary license pending next examination for graduates of approved medical schools.
Iowa	Resident physician license for training in approved hospital under supervision of licensed physician.
Kansas	Temporary permit until next board meeting. Not renewable. Appliaction must be in order for licensure.
Kentucky	Temporary permits issued to applicants by endorsement for six-month period to serve until investigations completed and meeting of board. Limited licenses *for one year, renewable for special place, purpose, and time.*
Louisiana	Temporary permit is granted to physicians possessing the necessary credentials who file application for examination or reciprocity and who locate in Louisiana between the regular semiannual meetings of the board. Temporary permit valid until next meeting of the board.
Maine	Temporary camp license for season. Hospital resident license for one year in specific hospital.
Massachusetts	Limited registration covering appointment as intern, resident or fellow in specific hospital, or as assistant in medicine while a student in medical school.
Michigan	Temporary annual license for resident training. Temporary annual license to Canadian citizens and foreign medical graduates who have fulfilled all the requirements for permanent licensure with the exception of full citizenship.
Minnesota	Limited license for duration of residency.
Mississippi	Temporary license for practice until next board meeting pending permanent license by examination or reciprocity. Temporary license is a full privilege license on temporary basis.
Montana	In extenuating circumstances in a community without adequate medical service, a temporary license may be issued until the next regular meeting of the board.
Nevada	Temporary permit for one year for residency training provided candidate is eligible for permanent licensure.
New Hampshire	Temporary license or until full citizenship or a maximum of five years for *foreign-trained physicians*; temporary license to residents in approved hospitals for duration of residency (optional).
New Jersey	Temporary license for four months to physicians eligible for full licensure when requested by licensed physician who will be out of the state.
New Mexico	Temporary permit issued until next board meeting. Institutional permit issued for practice in state hospitals only.
New York	Temporary certificate for two years for residency training except in state mental and municipal hospitals.
North Carolina	Limited license issued for duration of residency.
North Dakota	Temporary permit for United States and Canadian graduates until next board meeting.
Oklahoma	Temporary license for one year for residency training in approved hospital.
Pennsylvania	Postgraduate certificate issued for residency training in approved hospital and for the length of time required *for certification by a specialty board.*
Rhode Island	Temporary permit for one year for interns, residents, and house officers in hospitals.
South Carolina	Temporary permit for one year for interns, residents, residency training; renewable. Temporary permits are issued to endorsement applicants beginning practice prior to board meting.
South Dakota	Temporary license issued for graduates of foreign medical schools for four years for practice in emergency medical areas.
Texas	Temporary permit issued until next board meeting.
Vermont	Limited license for summer camp physicians.
Virginia	Temporary permit may be issued until next board meeting for reciprocity applicants.
Virgin Islands	Temporary certificate issued to military service personnel on duty, and to municipal personnel until next board meeting.
West Virginia	Temporary permit issued until next board meeting to qualified applicants.
Wisconsin	Temporary educational permit issued to graduates of foreign medical schools for residency training. May be renewed annually for not more than five years.

Schedule of Written Examination Dates and Reciprocity Meetings

The schedule of dates for written examination and meetings or oral examination for the issuance of licenses by reciprocity or by endorsement of credentials is given in table 23. In most instances, written examinations are scheduled twice annually and reciprocity meetings quarterly or as soon as the application for licensure can be processed. In those states requiring a basic science certificate for licensure, dates of the examination or reciprocity meetings are arranged closely timed with the examination and meeting dates of the boards of examiners in the basic sciences. A few states issue temporary permits enabling physicians to begin the practice of medicine until the board examination or meeting is held.

Table 21.—*Licensure, Registration, or Other Requirements for Interns*

Licensure	Registration	Other Requirements
Indiana	Arkansas	Arizona[1]
Puerto Rico	California	Florida[4]
Rhode Island[8]	Canal Zone	Pennsylvania[7]
South Carolina[8]	Colorado[2]	Virginia[9]
	Delaware[3]	West Virginia[10]
	District of Columbia[3]	
	Massachusetts[5]	
	Nebraska	
	New Jersey[6]	
	New Mexico	
	Texas	

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1. Licensed hospitals must register annually names of all interns.
2. May serve for an aggregate period not to exceed four years; required to register with licensing board annually.
3. May serve for two years without licensure.
4. Hospitals required to register names of interns every six months with State Board of Health. Interns may serve for a period of three years without licensure.
5. Limited registration granted.
6. May serve for not more than two years without licensure.
7. Hospitals required to report names of interns.
8. Temporary permit required.
9. Hospitals required to report names of interns and to secure permission from board to accept graduates of unapproved medical schools.
10. Graduates of foreign medical schools must obtain approval from board.

Medical License Fees

The fee charged by each of the medical licensing boards for registration by examination and by reciprocity or endorsement of credentials is given in table 24. The examination fee is nearly uniform throughout the country, the majority of the boards charging a fee of $25. Two boards reported an increase in the fee charged for the written examination, and three boards reported an increase in the fee charged for a license without written examination. Four boards—District of Columbia, Missouri, Oregon, and Tennessee—have a lower fee for those being certified on the basis of the certificate of the National Board of Medical Examiners than for candidates licensed by endorsement of state licenses. Kansas and North Dakota specify that the fee for a license without examination shall be a sum equal to the fee of the endorsing state.

Annual Registration

Forty boards require physicians to register their licenses annually or biennially. In table 25 are listed the licensing boards that exact this requirement and the fee charged for such registration. Some of these states require such registration whether or not the physician resides in the state. The fee charged ranges from $1 to $10. Six states have a nonresident fee. In Florida, physicians are required to register with the State Board of Health, whereas Illinois, New Hampshire, New York, North Carolina, and West Virginia require biennial registration.

Citizenship Requirements for Licensure

The requirements pertaining to United States citizenship exacted by various medical licensing boards are tabulated in table 26. Nine boards have no requirement for citizenship; 17 boards require the applicant for licensure to have declared his intention of becoming a United States citizen; 29 boards require the applicant for licensure to be a full citizen.

Table 22.—*Licensure, Registration, or Other Requirements for Residents*

Licensure	Registration	Other Requirements
Illinois[4]	Arkansas	Arizona[1]
Indiana	California	Florida[3]
Iowa[5]	Canal Zone	New Jersey[9]
Maine[6]	Colorado[2]	Pennsylvania[12]
Michigan[9]	Delaware	Virginia[14]
Minnesota[8]	District of Columbia	West Virginia[15]
Nevada[5]	Idaho	Wisconsin[16]
New York[10]	Massachusetts[7]	
North Carolina[11]	Nebraska	
Oklahoma[11]	New Mexico	
Puerto Rico		
Rhode Island[6]		
South Carolina[13]		
South Dakota		
Texas		

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1. Licensed hospitals must register annually names of all residents.
2. May serve for an aggregate period not to exceed four years; required to register with licensing board annually.
3. Hospitals required to register names of residents every six months with State Board of Health. Residents may serve for a period of three years without licensure.
4. Applicants who wish to serve residencies in Illinois hospitals and who are not eligible for permanent registration may apply for temporary certificates which are issued without examination. Temporary permit issued for service in state hospitals to physicians eligible for licensure.
5. Resident physician's license issued for a period of not more than seven years in approved hospital; must practice under the supervision of a licensed physician.
6. Temporary license issued.
7. Limited registration covering appointment as resident, or fellow in a specific hospital.
8. Temporary permit for one year; candidate must be eligible for permanent licensure.
9. May serve two years without licensure.
10. Temporary certificate for two years for residents, except in state mental and municipal hospitals.
11. Limited license for duration of residency.
12. Postgraduate certificate issued for residency training if licensed in any state or Canada or hold the certificate of the National Board of Medical Examiners.
13. Temporary permit for one year.
14. Hospitals required to report name of residents and to secure permission from board to accept graduates of unapproved medical schools.
15. Graduates of foreign medical schools must obtain approval from board.
16. Temporary educational permit issued to graduates of foreign medical schools.

Licensure on Government Credentials

In most of the states, no provision is made in the medical practice act for the acceptance of government credentials as a basis for licensure, without examination. Twelve boards—Alabama, Arizona, California, Canal Zone, Delaware, Guam, Illinois, Pennsylvania, Texas, Utah, Vermont, and Wisconsin—have indicated that, in their discretion, they may accept such credentials under varying regulations.

Registration Policies for Citizens of Canada by Licensing Boards in the United States

The licensing boards have reported that they will accept graduates of approved medical schools of Canada for licensure by examination on the same basis as graduates of approved medical schools of the United States. Table 27 records the registration policies for citizens of Canada. Few states indicate that they will accept Canadian registration for licensure by reciprocity or endorsement. Modifications are made, in some instances, in the citizenship requirement for candidates from Canada. This table shows for each state whether United States citizenship is a requirement, whether the candidate must declare his intention of becoming a citizen, or if no citizenship requirement is exacted.

TABLE 23.—*Schedule for Written Examination and Issuance of Licenses by Reciprocity or Endorsement of Credentials*

	Written Examinations	Licenses by Reciprocity or Endorsement Issued
Alabama	Annually	Continuously
Alaska	On application	On application
Arizona	Quarterly	Quarterly
Arkansas	June and November	June and November
California	Quarterly	Continuously
Canal Zone	On application	On application
Colorado	Twice annually	Quarterly
Connecticut	March, July, and November	Continuously
Delaware	January and July	January and July
District of Columbia	Twice annually	Quarterly
Florida	June and November	No Reciprocity
Georgia	June and October	June and October
Guam	On application	On application
Hawaii	January and July	Continuously
Idaho	Twice annually	Twice annually
Illinois	Quarterly	Quarterly
Indiana	Annually, June	Approximately 8 times annually
Iowa	June and December	Monthly
Kansas	January and June	January and June
Kentucky	Semiannually	Every two months
Louisiana	June and December	June and December
Maine	March, July, and November	March, July, and November
Maryland	June and December	Every five weeks
Massachusetts	January and July	Monthly except August
Michigan	June and October	Continuously
Minnesota	Quarterly	Quarterly
Mississippi	Annually in June	June and December
Missouri	Three times annually	Six times annually
Montana	Semiannually	Semiannually
Nebraska	Annually in June	Continuously
Nevada	Quarterly	Quarterly
New Hampshire	Twice annually	Twice annually
New Jersey	June and October	Monthly except August
New Mexico	Twice annually	Twice annually
New York	June and December	Continuously
North Carolina	Annually	Five times annually
North Dakota	January and July	January and July
Ohio	June and December	January, April, June, July, October, and December
Oklahoma	Annually	Quarterly
Oregon	January and July	Quarterly
Pennsylvania	January and July	Every six weeks
Puerto Rico	Twice annually	Continuously
Rhode Island	Quarterly	Eight times annually; special meetings
South Carolina	Twice annually	Three times annually
South Dakota	Twice annually	Continuously
Tennessee	Quarterly	Continuously
Texas	Twice annually	Quarterly
Utah	Once annually	February, June, August, and November
Vermont	January and June	Continuously
Virgin Islands	Twice annually	Twice annually
Virginia	Twice annually	Twice annually
Washington	January and July	January and July
West Virginia	January and July	Quarterly
Wisconsin	January and July	Quarterly
Wyoming	Three times annually	Three times annually

TABLE 24.—*Medical Licensure Fees*

	Examination	Reciprocity or Endorsement
Alabama	$ 25	$ 50
Alaska	35	110
Arizona	25	100
Arkansas	25	100
California	25	100
Canal Zone	10	5
Colorado	25	50
Connecticut	50	100
Delaware	25	100
District of Columbia	25	50[a]
Florida	50	..
Georgia	20	[illegible]
Guam	50	50
Hawaii	50	50
Idaho	25	100
Illinois	75	50[b]
Indiana	25	100
Iowa	25	50
Kansas	50	..[c]
Kentucky	50	75
Louisiana	25	15
Maine	27	52
Maryland	50	100
Massachusetts	50	75
Michigan	30	100
Minnesota	25	100
Mississippi	10	35
Missouri	25	100[a]
Montana	50	75
Nebraska	25	50
Nevada	100	200
New Hampshire	30	50
New Jersey	50	100
New Mexico	50	50
New York	40	40
North Carolina	50	100
North Dakota	100	..[c]
Ohio	50	100
Oklahoma	25	100
Oregon	50	100[d]
Pennsylvania	25	50
Puerto Rico	30	30
Rhode Island	20	20
South Carolina	25	100
South Dakota	20	50
Tennessee	35	50[e]
Texas	50	100
Utah	25	50
Vermont	20	50
Virginia	50	100
Virgin Islands	65	65
Washington	25	25
West Virginia	25	100
Wisconsin	50	100
Wyoming	50	50

a. Endorsement fee, $25.
b. Clinical Test, $50.
c. Sum equal to fee of endorsing state.
d. Endorsement fee, $50.
e. Endorsement fee, $10.

Licensure of Foreign-trained Physicians

The Council on Medical Education and Hospitals of the American Medical Association and the Executive Council of the Association of American Medical Colleges for a period of ten years (1950-1960) published a listing of foreign medical schools whose graduates they have recommended for consideration on the same basis as graduates of approved medical schools in the United States and Canada. This list was offered as an advisory list for the use of state licensing boards, hospitals, specialty boards, and other organizations, in the United States concerned with the evaluation of medical schools. It was acknowledged that this was a tentative listing and that the position of the two councils with respect to foreign medical schools not listed was that they neither approved nor disapproved them. With the development and operation of the American Medical Qualifying Examination by the Educational Council for Foreign Medical Graduates (referred to elsewhere in this study), both councils have withdrawn this listing, effective January 1, 1960. The councils wish to emphasize that this notice of discontinuing the listing of foreign medical schools is not intended to indicate any lowering of standards of the foreign medical schools that have been on the list. Rather, this action reflects the councils inability to acquire and maintain a continuing, adequate knowledge of the educational programs of the foreign medical schools whose graduates come to the United States.

TABLE 25.—*States Requiring Annual Registration*

State	Fee	State	Fee
Alabama	$ 5.00	Nebraska	$ 3.00
Alaska	10.00	Nevada	10.00
Arizona	5.00	New Hampshire*	5.00
Arkansas	a	New Mexico	f
California	3.00	New York*	6.00
Colorado	b	North Carolina*	5.00
Connecticut	5.00g	North Dakota	5.00
District of Columbia	4.00	Oklahoma	5.00
Georgia	3.00	Oregon	g
Hawaii	5.00	Pennsylvania	1.00
Idaho	10.00	Rhode Island	1.00
Illinois*	6.00	South Dakota	2.00
Indiana	d	Tennessee	5.00
Iowa	3.00	Texas	5.00
Kansas	5.00	Utah	3.00
Louisiana	10.00	Vermont	2.00
Maryland	5.00	Virginia	1.00
Michigan	5.00	Washington	7.00
Minnesota	3.00	West Virginia*	2.00
Missouri	2.50	Wisconsin	3.00
Montana	e	Wyoming	2.50

* Biennial Registration.
a. Residents $2, nonresidents $4.
b. Residents $2, nonresident $10.
c. Required by State Board of Health.
d. Residents $5, nonresidents $10.
e. Residents $5, nonresidents $1.
f. Residents $2, nonresidents $5.
g. Residents $20, nonresidents $5.

TABLE 26.—*Citizenship Requirements for Permanent Licensure*

No Requirement

California
Canal Zone
District of Columbia
Guam
Maine
North Dakota
Utah
Virgin Islands
Washington

Declaration of Intention

Arizona
Connecticut
Hawaii
Idaho
Indiana
Iowa
Maryland
Massachusetts
Mississippi
New York
Oregon
Pennsylvania
Rhode Island
South Dakota
Texas
Virginia
Wisconsin

Full Citizenship

Alabama
Alaska
Arkansas
Colorado
Delaware
Florida
Georgia
Illinois
Kansas
Kentucky
Louisiana
Michigan
Minnesota
Missouri
Montana
Nebraska
Nevada
New Hampshire
New Jersey
New Mexico
North Carolina
Ohio
Oklahoma
Puerto Rico
South Carolina
Tennessee
Vermont
West Virginia
Wyoming

The two councils now recommend that agencies in the United States concerned with the medical qualifications of graduates of foreign medical

TABLE 27.—*Registration Policies for Citizens of Canada by Licensing Boards in the United States*

	Graduates of Approved Canadian Medical Schools Considered for Licensure by Examination on Same Basis as Graduates of Approved Medical Schools in United States	Graduates of Approved Canadian Medical Schools Presenting Canadian Registration Acceptable for Licensure by Reciprocity or Endorsement	Graduates of Medical Schools Outside of United States and Canada Presenting Canadian Registration Accepted for Licensure by Reciprocity or Endorsement on Such Credentials	United States Citizenship Requirement for Candidates from Canada		
				Full Citizenship	Declaration of Intention	Not Required
Alabama	x	..	..	..	..	x
Alaska	x	..	..	x	..	..
Arizona	x	..	..	..	x	..
Arkansas	x	..	..	x	..	..
California	x	..	..	..	..	x
Canal Zone	x	x	x	..	..	x
Colorado	x	..	..	x	..	..
Connecticut	x	x	..	..	x	..
Delaware	x	..	..	..	x	..
District of Columbia	x	..	..	..	..	x
Florida	x	..	..	x	..	..
Georgia	x	..	..	x	..	..
Guam	x	..	..	..	..	x
Hawaii	x	..	..	..	x	..
Idaho	x	..	..	x	..	..
Illinois	x	..	..	x	..	..
Indiana	x	..	..	..	..	x
Iowa	x	x	..	..	x	..
Kansas	x	..	..	x	..	..
Kentucky	x	..	..	x	..	..
Louisiana	x	..	..	..	x	..
Maine	x	..	..	..	..	x
Maryland	x	..	..	..	..	x
Massachusetts	x	..	..	..	x	..
Michigan	x	..	..	..	x[1]	..
Minnesota	x	..	..	..	..	x
Mississippi	x	x	..	..	..	x
Missouri	x	..	..	x	..	..
Montana	x	..	..	..	x	..
Nebraska	x	..	..	x	..	..
Nevada	x	..	..	..	x	..
New Hampshire	x	x	..	..	..	x
New Jersey	x	..	..	x	..	..
New Mexico	x	..	..	x	..	..
New York	x	..	..	..	x	..
North Carolina	x	..	..	x	..	..
North Dakota	x	..	..	..	x[1]	..
Ohio	x	..	..	..	x	..
Oklahoma	x	..	..	x	..	..
Oregon	x	..	..	..	..	x
Pennsylvania	x	..	..	..	x	..
Puerto Rico	x	..	..	x	..	..
Rhode Island	x	..	..	..	x	..
South Carolina	x	..	..	x	..	..
South Dakota	x	..	..	..	x	..
Tennessee	x	..	..	x	..	..
Texas	x	..	..	..	x	..
Utah	x	..	..	..	..	x
Vermont	x	x	..	..	..	x
Virgin Islands	x	..	..	..	..	x
Virginia	x	..	..	x	..	..
Washington	x	x	..	..	..	x
West Virginia	x	..	..	x	..	..
Wisconsin	x	..	..	x	..	..
Wyoming	x	x	..	x	..	..

x Implies Yes
[1] Issued temporary license renewable for five years or until full citizenship is obtained.

schools consider certification by the Educational Council for Foreign Medical Graduates as evidence that the recipient of such certification is possessed of medical knowledge comparable to that expected of graduates of approved medical schools in the United States and Canada. These two councils further recommend that such certification be considered as evidence of the quality of medical training offered by the medical school attended by the holder of a certificate at the time of his graduation.

The current requirements for foreign-trained physicians seeking medical licensure in the United States and its possessions are given in table 28. Foreign-trained physicians are not eligible for licensure in Arkansas, Louisiana, Nevada, Oklahoma, Utah, and Wyoming. All but 13 boards have the requirement that the applicant must present the certificate obtained after successfully passing the American Medical Qualifying Examination of the Educational Council for Foreign Medical Graduates. A column in the table indicates the states which exact this requirement. The citizenship requirement of each board is specified in this table as well as separately in table 26. Thirty-two boards reported that the foreign-trained physician must serve an internship of one year or more in an approved hospital in the United States before being eligible for licensure. In addition to the items tabulated in this table, many of the boards have specific requirements or varying exemptions. The factual data pertaining to these regulations are included in the text.

This chart was developed by the Council on Medical Education and Hospitals of the American Medical Association in an effort to assist the foreign-trained physician seeking licensure in the United States. An attempt has been made to present the situation as it exists; the table is intended to give only a summary of existing requirements. Persons interested in licensure should supplement these data by communicating with the licensing boards. Medical licensure in the United States is a "state right" and is entirely under the jurisdiction of the governments of the individual states. The power to license physicians is exercised through the medical licensing board of each state. Official supplementary information concerning the acceptability of foreign credentials and subsequent changes in the regulations should be obtained directly from the licensing board. There is also available from the office of either Council a pamphlet entitled "The Present and Future Status of Foreign Medical School Credentials in the United States," which contains helpful information to foreign-trained physicians.

Table 29 records the number of graduates of foreign faculties of medicine examined for medical licensure by 43 boards in 1959. The figures include both foreign-born and American citizens educated abroad. Graduates of medical schools of the Philippines, Iceland, 18 South and Central American countries, 21 European countries, and 21 countries in Asia and Africa were represented at examination. The number of examinees totaled 2,766. Graduates of 244 medical schools were examined. The number who were successful was 1,870; failures numbered 896 (32.4%). More than 75 graduates from seven schools were examined, and 19 schools had from 25 to 75 of their graduates examined for licensure in the United States in 1959.

The greatest number examined by any one state was 613 in New York; 343 passed, and 270 (44%) failed. Illinois examined the next greatest number 574; 345 passed, and 229 (39.8%) failed. More than 100 were also examined in California, Connecticut, New Jersey, Ohio, and Virginia.

Table 30 presents the number of graduates of foreign faculties of medicine examined for medical licensure in the United States in 30 years (1930-1959). In 1936, the number of foreign-trained physicians seeking licensure in the United States began to increase; by 1940, there were over three times as many as were tested in 1936. Beginning in 1944, the number examined began to decrease, until 1951, when there was a noticeable increase. In each succeeding year, the number examined has increased. In 1959, the increase over the previous year was 199. At no time in the 30-year period did fewer than 30% fail. The percentage of failures in 1959 was the lowest in 22 years.

In table 31 are given, for a 14-year period (1946-1959), the number of foreign-trained physicians licensed by each state board, both after written examination and by endorsement of credentials. Whereas table 29 reflects the candidates registered after examination only and indicates the percentage failing in each year, table 31 records the total number licensed in each state. In the period from 1946 to 1959, there were 11,187 licenses issued to foreign-trained physicians after written examination and 2,322 by endorsement of credentials. The total number of such licentiates registered was 13,509.

Represented in table 32 are figures regarding the foreign-trained physicians registered in 1959 who were not previously licensed in the United States and who, therefore, are additions to the medical profession. There were 1,626 in this group. Of these, 1,605 were licensed by written examination and 21 by endorsement of credentials. Comparative figures for nine previous years, together with the figures for 1959, are given in table 33. In ten years (1950-1959), there were 8,349 foreign-trained physicians who were added to the physician population of the United States. Of these, 8,088 obtained licensure by written examination and 261 by endorsement of credentials.

TABLE 28.—*Status of Requirements for Medical Licensure for Physicians Trained in Foreign Countries Other than Canada**

	Written Examination Required	Admitted Also on Reciprocal or Endorsement Basis	Citizenship	Basic Science Certificate	Internship in United States	Required to Pass Examination of Educational Council for Foreign Medical Graduates	Additional Requirements	Examination Fee, Dollars
Alabama	x	..	x	x	x	x	x	25
Alaska	x	x	x	x	x	..	..	35
Arizona	x	..	D	x	x	x	..	25
Arkansas	Not Accepted							
California	x	..	..	..	x	..	x	25
Canal Zone	x	x	..	..	..	..	x	10
Colorado	x	..	x	x	x	..	x	25
Connecticut	x	..	D	x	..	x	x	35
Delaware	x	x	x	..	x	x	x	25
District of Columbia	x	x	..	x	x	..	..	25
Florida	x	..	x	x	..	x	..	50
Georgia	x	x	x	..	..	x	..	20
Guam	x	x	..	..	x	x	..	50
Hawaii	x	x	D	..	x	..	x	50
Idaho	x	..	D	..	x	x	x	25
Illinois	x	..	x	..	x	..	x	50
Indiana	x	..	D	..	..	..	x	25
Iowa	x	..	D	x	x	x	..	25
Kansas	x	x	x	x	x	..	x	50
Kentucky	x	..	x	..	x	x	x	50
Louisiana	Not Accepted							
Maine	x	x	..	..	x	x	..	27
Maryland	x	..	D	..	x	x	x	35
Massachusetts	x	..	D	..	..	..	x	50
Michigan	x	..	D	x	x	x	x	30
Minnesota	x	..	x	x	x	x	x	25
Mississippi	x	..	D	..	..	x	x	10
Missouri	x	..	x	..	x	x	..	25
Montana	x	x	x	..	x	x	..	50
Nebraska	x	..	x	x	..	x	..	25
Nevada	Not Accepted							
New Hampshire	x	..	x	..	x	x	x	30
New Jersey	x	x	x	..	x	..	x	50
New Mexico	x	..	D	x	..	x	..	50
New York	x	..	D	..	..	..	..	40
North Carolina	x	..	x	..	..	x	x	50
North Dakota	x	..	D	..	x	x	x	50
Ohio	x	..	x	..	..	x	x	50
Oklahoma	Not Accepted							
Oregon	x	..	D	x	x	x	x	50
Pennsylvania	x	..	D	..	x	x	x	25
Puerto Rico	x	..	x	..	x	..	..	30
Rhode Island	x	x	D	x	x	x	x	25
South Carolina	x	..	x	..	..	..	x	75
South Dakota	x	..	D	x	x	x	x	20
Tennessee	x	x	x	x	..	..	x	35
Texas	x	..	D	x	..	x	..	50
Utah	Not Accepted							
Vermont	x	..	x	..	x	x	x	20
Virgin Islands	x	..	..	..	x	..	x	65
Virginia	x	..	D	..	x	x	x	50
Washington	x	x	..	x	x	x	..	25
West Virginia	x	..	x	..	x	x	x	25
Wisconsin	x	x	D	x	x	x	x	75
Wyoming	Not Accepted							

This summary should be supplemented by direct communication with the secretary of the licensing board of the state in which the physician is interested

* See separate table applicable to Canadian citizens.
x Implies yes.
D Declaration of intention to become citizen of the United States.

Additional Requirements

Alabama. Candidate is eligible if he is certified by the National Board of Medical Examiners and approved.

California. Two-year internship is an approved hospital in the United States, one of said years being in California.

Canal Zone. Acceptable at the discretion of the Board of Medical Examiners.

Colorado. Credentials must be submitted in original form and accompanied by translation and will be directly verified or documents should bear evidence of being visaed by the U. S. Consul in the country wherein the school of graduation is or was located.

Connecticut. Minimum of three years of hospital training in approved hospital in United States or Canada required, one year of which must be in general medicine.

Delaware. Residence for one year required.

Georgia. Reciprocity applicants may furnish certification of passing examination of Educational Council for Foreign Medical Graduates in lieu of acceptable medical school, and applicants for examination are given consideration on an individual basis.

Hawaii. Residence for one year required. Diplomates of National Board eligible on reciprocity basis.

Idaho. Considered on an individual basis.

Illinois. Limited license for practice in hospitals maintained by the state.

Indiana. Two years postgraduate training in approved hospital in United States required.

Kansas. Certificate from medical college specifying in detail the physical equipment of the school, the curriculum, current catalog showing courses of study, and certificate that the college is recognized by authorities of such foreign country as qualifying its graduates for practice therein; diploma from such college; certificate of licensure in the country where graduated; all documents to be translated into English and certified by the consul.

Kentucky. Applicant required to complete at least five years' training in the United States in an institution approved by the board and to have successfully passed examination of National Board of Medical Examiners.

Maryland. Three years hospital service in the United States required, one year of which must be a rotating internship or one year of residency in internal medicine; also one of the three years must have been spent in an approved hospital in Maryland.

Massachusetts. Must furnish documentary evidence that education is equivalent to that of graduates of United States medical schools and shall be required to take examination of National Board of Medical Examiners who shall certify that the applicant has successfully passed said examination.

Michigan. Temporary licenses for private practice may be granted to those foreign medical graduates who have served an approved internship in Michigan and have declared their intention to become a citizen of the United States.

Minnesota. Two-year internship is required.

Mississippi. Interview by examining board prior to examination required.

New Hampshire. Diplomates of National Board of Medical Examiners eligible on endorsement basis. Temporary license valid until citizenship *is completed may be given. Considered on an individual basis.* Certified copies of credentials and translations must be filed with *application.*

New Jersey. Candidates graduated after June 30, 1950 required to have not less than three years of training in a hospital approved by the board.

North Carolina. Considered on an individual basis.

North Dakota. Considered on an individual basis. Must be licensed in country of school of graduation.

Ohio. Must serve at least two years as intern or resident in approved hospital in United States.

Oregon. The board at its discretion may utilize the facilities of the Educational Council for Foreign Medical Graduates. Must show evidence of internship and/or residency of not less than two years in not more than two hospitals approved for such training. Less than an unqualified recommendation from the heads of these training programs shall preclude further consideration.

Pennsylvania. Graduates of foreign medical schools, with the exception of those who maticulated before Oct. 1, 1957 in the schools approved *by the board* or those licensed by examination in another state, are required to pass the examinations of Educational Council for Foreign Medical Graduates.

South Carolina. Physicians holding foreign diplomas who are Board certified or Board eligible in their specialty and who received this training in the United States eligible. Permanent license issued to full citizens. Temporary permits issued on a yearly basis to those who have not received their final citizenship papers.

South Dakota. Applicant required to practice in an emergency area for four years under a temporary license and reappear before the board *for permanent licensure.*

Tennessee. All applicants must be from medical schools whose curriculum equals that of the University of Tennessee. Each applicant considered on an individual basis.

Virgin Islands. Residence of six months required.

Virginia. Applicant must be licensed to practice medicine and surgery in country in which school of graduation is located or must have completed the course of study and passed examinations equivalent to those required for a diploma or license conferring such full right to practice. Two years of internship in approved hospital in the United States or Canada within the past five years prior to application. If citizenship is not acquired within seven years after licensure, the license automatically becomes void.

West Virginia. Applicant must be resident of the state for three years preceding application and recommended by local society.

Wisconsin. 1953 Legislature established One Year Temporary Educational Permit, which authorizes graduates of unapproved foreign schools to obtain residency training in approved hospitals. May be renewed for two additional years.

TABLE 29.—*Foreign Trained Physicians Exa*

Marginal Number	SCHOOL	1 Arizona		2 California		3 Colorado		4 Connecticut		5 Delaware		6 District of Columbia		7 Florida		8 Georgia		9 Hawaii		10 Illinois		11 Indiana		12 Iowa		13 Kansas		14 Maine		15 Maryland		16 Massachusetts	
		P	F	P	F	P	F	P	F	P	F	P	F	P	F	P	F	P	F	P	F	P	F	P	F	P	F	P	F	P	F	P	F
	ARGENTINA																																
1	Universidad Nacional de Buenos Aires Facultad de Ciencias Medicas			1	0															4	0												
2	Universidad Nacional de Cordoba Facultad de Ciencias Medicas							1	0											1	0												
3	Universidad Nacional del Litoral Facultad de Ciencias Medicas,																																
4	Ur[illegible] La Plata Escuela de Ciencias Medicas																			0	1							1	0				
	AUSTRALIA																																
5	University of Melbourne Faculty of Medicine			1	0																												
6	University of Sydney Medical School																																
7	University of Queensland Medical School, Brisbane																															1	1
8	University of Adelaide Faculty of Medicine																															1	0
	AUSTRIA																																
9	Karl-Franzens [illegible] akultat, Graz							0	1							1	0			3	3									1	0		
10	Leopold Franz[illegible] Fakultat, Innsbruck			1	0			1	1			1	0							7	4							2	0	1	0	0	1
11	Medizinische Fakultat der Universitat Wien			5	1			1	2											2	1							1	0				
	BELGIUM																																
12	Universite Libre de Bruxelles Faculte de Medecine					1	0	3	1																								
13	Universiteit Gent Faculteit der Geneeskunde also Universite de Gand Faculte de [illegible]							2	0			1	0																				
14	Universite Catholique [illegible]							2	0			1	0							3	1	2	0										
	BOLIVIA																																
15	Universidad Mayor de San Andres Facultad de Ciencias Medicas, La Paz																			1	0												
16	Universidad de San Simon Facultad de Medicina, Cochabamba			1	0																												
	BRAZIL																																
17	Faculdade de Medicine Cirurgia e Pharmacia, Bahia																																
18	Universidade do Brazil Faculdade de Medicine, Cirurgia e Pharmacia, Rio de Janeiro							1	1											2	0											0	2
19	Universidade de Parana Faculdade de Medicine, Curitiba																					1	0							0	1	0	1
	BULGARIA																																
20	University of Sofia Faculty of Medicine																																
	CHILE																																
21	Universidad de Chile, Facultad de Ciencias Medicas, Santiago							1	0																								
	CHINA																																
22	National Peking University, Peking																																
23	*Hsiang Ya* Medical College, Changsha																																
24	Pennsylvania Medical School, Medical Department of St. John's University, [illegible]																			1	0											1	0
25	Cheeloo University Sc[illegible]																																
26	National College of Medicine of Shanghai							1	0													1	1			1	0			1	0	1	0
27	West China Union University [illegible] ngtu,			1	0															2	0					1	0						
28	D[illegible] nton			1	0			0	1																			1	0				
29	A[illegible]							0	1																								
30	Mi[illegible] Medical College, Nanking																			0	1												
31	National Central University College of Medicine, Nanking																															1	0
32	National Tung Chi University College of Medicine, Shanghai, [illegible]																	1	0														
33	N[illegible]																																
34	Sh[illegible]			1	0																											0	1
35	Fukien Provincial Medical College, Foochow, Fukien			0	1																												
36	Shansi University Medical College, Taiyuan, Shansi																																
37	Tung Teh Medical School, Shanghai																																
38	Hopeh Provincial College of Medicine, Paoting																			1	1												
	CHOSEN																																
39	Severance Union Medical College, Keijo, Chosen							1	0																								
	COLOMBIA																																
40	Universidad Nacional Facultad de Medicina, Bogota			1	0									2	1	1	0			1	0												
41	Universidad de Cartagena Facultad de Medicina, Cartegena																																
42	Universidad de Antioquia Facultad de Medicina y Ciencias Naturales, Medellin																																
	CUBA																																
43	Universidad de la Habana Facultad de Medicina Y Farmacia			1	1			1	1					6	2	9	2			61	38	1	0							2	0	0	2
	CZECHOSLOVAKIA																																
44	Deutsche Universitat Medizinische Fakultat, Prag																			1	1												
45	Universita Karlova Fakulta Lekarska, Praha			2	1			1	1											5	3												
46	Univerzita Komenskeho Fakulta Lekarska, Bratislava													1	0																		
47	Masarykova Universita Fakulta Lekarska, Brno																			0	1												
	DENMARK																																
48	Kobenhavns Universitet Laegevidenskabelige Fakultet			1	0			1	1																								
	DOMINICAN REPUBLIC																																
49	Universidad de Santo Domingo Facultad de Medicina			0	2			1	1											14	9									1	0		
	ECUADOR																																
50	Universidad Central Facultad de Ciencias Medicas, Quito													0	1					4	3												
	EGYPT																																
51	Egyptian University Faculty of Medicine, Cairo																			5	0									1	0	1	1
52	Fouad First University Faculty of Medicine, Cairo			1	0																												
53	Alexandria University Faculty of Medicine, Alexandria																			2	0												
54	University of Ein Shams, Abbasia Faculty of Medicine, Sharia El-Malikia, Cairo			1	0																												
	EL SALVADOR																																
55	Universidad de El Salvador Facultad de Medicina, San Salvador																			0	1												
	ENGLAND																																
56	University of Birmingham Faculty of Medicine			1	0															1	0									1	0		
57	University of Cambridge Faculty of Medicine							1	0					1	0																	1	0
58	University of Durham Medical School, Kings College, Newcastle-upon-Tyne							2	1			1	0																	1	0	2	
Marginal Number		1		2		3		4		5		6		7		8		9		10		11		12		13		14		15		16	

P—Passed; F—Failed

19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40	41	42	43	44	45	
Mississippi	Missouri	Montana	Nebraska	New Hampshire	New Jersey	New Mexico	New York	North Carolina	North Dakota	Ohio	Oregon	Pennsylvania	Rhode Island	South Dakota	Tennessee	Texas	Virginia	Washington	West Virginia	Wisconsin	Canal Zone, Guam, Puerto Rico, Virgin Islands	Totals	Examined—Passed	Examined—Failed	Percentage Failed	Number of Boards Examined by	Marginal Number
P F	P F	P F	P F	P F	P F	P F	P F	P F	P F	P F	P F	P F	P F	P F	P F	P F	P F	P F	P F	P F	P F						
....	....	....	....	....	2 0	....	2 1	....	....	....	....	1 0	1 0	....	....	....	4 1	....	....	....	1 0	18	16	2	11.1	8	1
....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	2	2	0	0.0	2	2
....	1 0	....	....	....	....	....	....	....	....	....	....	....	....	....	....	1 0	....	....	....	....	....	3	3	0	0.0	3	3
....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	1	0	1	100.0	1	4
....	....	....	....	....	....	....	3 0	....	....	....	....	....	....	....	....	....	....	....	....	....	....	4	4	0	0.0	2	5
....	2 0	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	4	3	1	25.0	2	6
....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	1	1	0	0.0	1	7
....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	1 0	....	....	....	....	1	1	0	0.0	1	8
....	1 0	....	....	....	....	....	2 2	....	....	1 1	....	....	0 1	....	....	....	....	....	....	....	....	17	9	8	47.1	8	9
....	....	....	....	....	2 0	....	1 1	....	....	2 0	....	1 0	1 0	0 1	....	0 1	2 0	....	1 0	....	....	35	26	9	25.7	18	10
....	....	....	....	....	1 1	....	4 12	....	....	3 3	....	2 0	....	1 0	....	....	2 1	0 2	1 0	....	....	47	24	23	48.9	13	11
....	....	....	....	....	....	....	0 2	....	....	1 0	....	....	....	....	....	....	....	....	....	....	....	8	5	3	37.5	4	12
....	....	....	....	....	....	....	....	....	....	....	....	2 0	....	....	....	1 0	....	....	....	....	....	6	6	0	0.0	4	13
....	....	....	1 0	....	....	....	2 0	....	....	2 0	....	3 0	....	....	1 0	....	....	0 1	....	....	....	19	17	2	10.5	10	14
....	....	....	....	....	....	....	0 1	....	....	....	....	....	....	....	....	....	....	....	....	....	....	2	1	1	50.0	2	15
....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	1	1	0	0.0	1	16
....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	1 0	....	....	....	....	....	1	1	0	0.0	1	17
....	....	....	....	....	....	....	1 2	....	....	....	....	....	1 0	....	....	....	....	....	....	....	....	10	5	5	50.0	5	18
....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	3	1	2	66.7	3	19
....	....	....	....	....	1 0	....	....	....	....	1 2	....	....	....	....	....	....	....	....	....	....	....	4	2	2	50.0	2	20
....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	1 0	....	....	....	....	2	2	0	0.0	2	21
....	....	....	....	....	....	....	1 0	....	....	....	....	....	....	....	....	....	....	....	....	1 0	....	2	2	0	0.0	2	22
....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	1 0	....	....	....	....	....	1	1	0	0.0	1	23
....	....	....	....	....	....	....	1 0	....	....	....	....	1 0	....	....	....	....	....	....	....	....	....	4	4	0	0.0	4	24
....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	1	1	0	0.0	1	25
....	....	....	....	....	....	....	2 0	....	....	1 0	....	....	1 0	....	....	....	1 0	....	....	....	....	11	10	1	9.1	9	26
....	....	....	....	....	....	....	....	....	....	....	....	1 0	....	....	....	....	0 1	....	....	....	....	6	5	1	16.7	5	27
....	....	....	....	....	0 2	....	....	....	....	1 0	....	1 0	....	....	....	....	1 0	....	....	....	....	8	5	3	37.5	7	28
....	....	....	....	....	....	....	0 1	....	....	....	....	....	....	....	....	1 1	....	....	....	....	....	4	1	3	75.0	3	29
....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	1	0	1	100.0	1	30
....	....	....	....	....	....	....	1 0	....	....	....	....	....	1 0	....	....	1 0	....	....	....	....	....	4	4	0	0.0	4	31
....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	1	1	0	0.0	1	32
....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	0 1	....	....	....	1	0	1	100.0	1	33
....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	2	1	1	50.0	2	34
....	....	....	....	....	....	....	0 1	....	....	....	....	....	....	....	....	....	....	....	....	....	....	2	0	2	100.0	2	35
....	....	....	....	....	....	....	1 0	....	....	....	....	....	....	....	....	....	....	....	....	....	....	1	1	0	0.0	1	36
....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	1	0	1	100.0	1	37
....	....	....	....	....	....	....	....	....	....	0 1	....	....	....	....	....	....	....	....	....	....	....	3	1	2	66.7	2	38
....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	1	1	0	0.0	1	39
....	....	....	....	....	1 0	....	....	....	....	....	....	....	....	....	....	....	1 0	....	....	....	....	8	7	1	12.5	6	40
....	....	....	....	....	....	....	2 0	....	....	....	....	....	....	....	....	....	....	....	....	1 0	....	3	3	0	0.0	2	41
....	....	....	....	....	....	....	1 0	....	....	....	....	1 0	....	....	....	....	....	....	....	....	....	2	2	0	0.0	2	42
....	2 0	....	....	....	0 1	....	0 4	....	....	3 2	....	....	1 0	....	....	2 0	2 5	....	....	....	0 2	153	93	60	39.2	17	43
....	....	....	....	....	....	....	5 5	....	....	....	....	....	....	....	....	....	....	....	....	....	....	12	6	6	50.0	2	44
....	....	....	....	....	....	....	3 5	....	....	0 1	....	....	....	....	....	....	1 0	....	....	1 0	....	24	13	11	45.8	7	45
....	....	....	....	....	....	....	0 1	....	....	....	....	....	....	....	....	....	....	....	....	....	....	2	1	1	50.0	2	46
....	....	....	....	....	....	....	1 1	....	....	....	....	....	....	....	....	....	....	....	....	....	....	3	1	2	66.7	2	47
....	....	....	....	....	....	....	1 0	....	....	....	....	....	....	....	....	....	....	0 1	....	....	....	5	3	2	40.0	4	48
....	....	....	....	....	1 0	....	....	....	....	....	....	....	....	....	....	....	3 0	....	....	....	9 1	42	29	13	31.0	7	49
....	....	....	....	....	....	....	1 1	....	....	4 0	....	....	....	....	....	....	....	1 1	....	....	....	16	10	6	37.5	5	50
....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	9	8	1	11.1	4	51
....	1 0	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	0 1	1 0	....	....	....	4	3	1	25.0	4	52
....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	3	3	0	0.0	2	53
....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	1	1	0	0.0	1	54
....	....	....	....	....	0 1	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	2	0	2	100.0	2	55
....	....	....	....	....	....	....	2 0	....	....	....	....	....	....	....	....	....	....	....	....	....	....	6	6	0	0.0	5	56
....	....	....	....	....	....	....	4 0	....	....	....	....	....	1 0	....	....	....	....	....	....	....	....	8	8	0	0.0	5	57
....	....	....	....	....	....	....	3 0	....	....	....	....	....	....	1 0	....	....	....	....	....	....	....	11	10	1	9.1	6	58
19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40	41	42	43	44	45	

	Marginal Number	1		2		3		4		5		6		7		8		9		10		11		12		13		14		15		16	
Marginal Number	SCHOOL	Arizona		California		Colorado		Connecticut		Delaware		District of Columbia		Florida		Georgia		Hawaii		Illinois		Indiana		Iowa		Kansas		Maine		Maryland		Massachusetts	
		P	F	P	F	P	F	P	F	P	F	P	F	P	F	P	F	P	F	P	F	P	F	P	F	P	F	P	F	P	F	P	F
59	University of Leeds School of Medicine																																
60	University of Liverpool Medical School							1	0																							1	[illegible]
61	University of London Faculty of Medicine							2	0											1	0									2	0	2	[illegible]
62	University of Manchester Faculty of Medicine																					1	0										
63	University of Oxford School of Medicine																																
64	University of Sheffield Faculty of Medicine							1	0											1	0												
65	Licentiate of the Royal College of Physicians of London, Member of the Royal College of Surgeons, England																			1	1							1	0				
66	Licentiate in Medicine, Surgery and Midwifery of the Apothecaries' Society							1	0																								
	ESTONIA																																
67	Tartu Ulikooli-Faculte de Medecine de l'Universite de Tartu			0	1															0	2												
	FRANCE																																
68	Universite de Lyon Faculte de Medecine et de Pharmacie																			1	0												
69	Universite de Montpellier Faculte de Medecine																																
70	Universite de Nancy Faculte de Medecine							3	1											5	3	1	0									0	2
71	Universite de Paris Faculte de Medecine																			1	0					1	0						
72	Universite de Strasbourg Faculte de Medecine																																
73	Universite de Toulouse Faculte de Medecine et de Pharmacie																																
	GERMANY																																
74	Friedrich-Wilhelms Universitat Medizinische Fakultat, Berlin							2	1									2	0	1	2												
75	Rheinische Friedrich-Wilhelms Universitat Medizinische Fakultat, Bonn			1	1			1	1											2	1												
76	Schlesische-Friedrich-Wilhelms Universitat Medizinische Fakultat, Breslau			1	0																												
77	Friedrich-Alexanders Universitat Medizinische Fakultat, Erlangen			2	0			2	2											2	1							1	0	1	0		
78	Albert-Ludwigs Universitat Medizinische Fakultat, Freiburg			0	1			1	0											1	1							1	0				
79	Georg August Universitat Medizinische Fakultat, Gottingen									1	0									2	0											1	2
80	Universitat Heidelberg Medizinische Fakultat, Baden			4	3			3	1											5	3					1	0	1	1	1	0	1	0
81	Thuringische Landesuniversitat Medizinische Fakultat, Jena			1	0															1	1												
82	Christian-Albrechts Universitat Medizinische Fakultat, Kiel			1	1			1	0					1	0					2	1									0	1		
83	Albertus Universitat Medizinische Fakultat, Konigsberg																																
84	Universitat Leipzig Medizinische Fakultat															1	0			0	1												
85	Philipps Universitat Medizinische Fakultat, Marburg																			2	2					1	0						
86	Ludwig-Maximilians Universitat Medizinische Fakultat, Munchen	1	0	1	1			3	0					1	0					6	15	1	0			1	0	0	2	1	1	1	0
87	Universitat Rostock Medizinische Fakultat																																
88	Eberhard-Karls Universitat Medizinische Fakultat, Tubingen							0	1											4	5							1	0	1	0		
89	Julius-Maximilians Universitat Medizinische Fakultat, Wurzburg																			1	1												
90	Hamburgische Universitat Medizinische Fakultat, Hamburg			1	0									1	0	1	0			5	4												
91	Universitat Koln Medizinische Fakultat			1	0			0	1											4	0												
92	Johann Wolfgang Goethe Universitat Medizinische Fakultat, Frankfurt-am-Main	0	1	1	0			2	1											4	4											1	0
93	Westfalische Wilhelms Universitat Medizinische Fakultat, Munster																			1	0	1	0										
94	Medizinische Akademie Dusseldorf			0	1																												
95	Humboldt University Medical School, Berlin																																
96	Medizinische Fakultat der Johannes Gutenberg Universitat, Mainz			1	0									1	0					1	1							1	0				
97	Freien Universitat Medizinische Fakultat, Berlin																																
	GREECE																																
98	National University of Athens School of Medicine			3	4			5	7											19	16							2	0	1	1	1	[illegible]
99	Aristotle University of Salonika Faculty of Medicine, Salonika							1	2																								
	GUATEMALA																																
100	Universidad Nacional de Guatemala Facultad de Ciencias Medicas																			0	1												
	HAITI																																
101	Ecole Nationale de Medecine et de Pharmacie, Port-au-Prince							1	0											1	2												
	HONDURAS																																
102	Universidad Central de la Republica de Honduras, Facultad de Medicina, Cirurgia y Pharmacia, Tegucigalpa			0	1																											0	1
	HONG KONG																																
103	University of Hong Kong Faculty of Medicine																													1	0		
	HUNGARY																																
104	Magyar Kiralyi Pazmany Petrus Tudomanyegyetem Orvosi Fakultasa, Budapest	2	0	4	2			1	0			1	0							16	5									3	0	1	0
105	Magyar Kiralyi Ferencz Josef Tudomanyegyetem Orvostudomanyi Kara, Szeged			0	1															3	0												
106	Magyar Kiralyi Erzsebet Tudomanyegyetem Orvostudomanyi, Pecs			1	1															1	0												
107	Magyar Kiralyi Tisza-Istvan-Tudomanyegyetem Orvosi Fakultasa, Debrecen																			5	1												
	ICELAND																																
108	Haskoli Islands Laec Knadeildin, Reykjavik																			1	0											0	1
	INDIA																																
109	University of Bombay																			1	1												
110	University of Calcutta							1	0											1	0												
111	University of Madras																															1	2
112	Lucknow University Faculty of Medicine																																
113	Mysore University Medical College																																
114	Medical College of Agra							0	1																								
115	University of Uthal Medical College, Cutack																			1	0												
116	Stanley Medical College, Madras																																
117	Prince of Wales Medical College, Patna, Bihar																													1	1		
118	Topewala National Medical College, Byculla, Bombay																																
119	Amritsar Medical College																																
	IRAN																																
120	Madresseh Teb (Government Medical School), Teheran			1	0			2	6			1	0	1	0					3	3							1	0	1	0		
	Marginal Number	1		2		3		4		5		6		7		8		9		10		11		12		13		14		15			

P—Passed; F—Failed

19 Mississippi P F	20 Missouri P F	21 Montana P F	22 Nebraska P F	23 New Hampshire P F	24 New Jersey P F	25 New Mexico P F	26 New York P F	27 North Carolina P F	28 North Dakota P F	29 Ohio P F	30 Oregon P F	31 Pennsylvania P F	32 Rhode Island P F	33 South Dakota P F	34 Tennessee P F	35 Texas P F	36 Virginia P F	37 Washington P F	38 West Virginia P F	39 Wisconsin P F	40 Canal Zone, Guam, Puerto Rico, Virgin Islands P F	41 Totals	42 Examined—Passed	43 Examined—Failed	44 Percentage Failed	45 Number of Boards Examined by	Marginal Number
...	...	...	...	...	...	...	1 0	...	...	...	...	...	...	...	...	...	...	...	...	...	...	1	1	0	0.0	1	59
...	...	...	...	...	...	...	2 0	...	...	...	...	...	...	...	...	...	...	...	...	...	...	4	4	0	0.0	3	60
...	...	...	...	...	...	...	10 1	...	...	...	...	2 0	...	1 0	...	1 0	...	...	...	...	...	22	21	1	4.5	8	61
...	...	...	...	...	...	...	3 0	...	...	...	...	...	1 0	...	...	...	1 0	...	...	...	...	7	7	0	0.0	5	62
...	...	...	...	...	...	...	4 0	...	...	...	...	...	...	...	...	...	...	1 0	...	...	...	5	5	0	0.0	2	63
...	...	...	...	...	...	...	2 0	...	...	...	...	1 0	1 0	...	...	...	...	...	...	1 0	...	7	7	0	0.0	6	64
...	1 0	...	...	...	...	...	1 1	...	...	...	...	1 0	...	...	...	...	...	0 1	...	...	...	8	5	3	37.5	6	65
...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	1	1	0	0.0	1	66
...	...	...	...	...	1 0	...	1 4	...	...	...	...	...	...	...	...	...	...	...	...	...	...	9	2	7	77.8	4	67
...	1 0	...	...	...	...	...	1 0	...	...	...	...	...	...	...	...	...	...	...	...	...	...	3	3	0	0.0	3	68
...	...	...	...	...	...	1 0	...	...	...	0 1	...	...	...	...	...	...	...	...	...	...	...	2	1	1	50.0	2	69
...	...	...	...	...	...	...	0 1	...	...	...	...	...	...	...	...	...	...	...	...	...	...	1	0	1	100.0	1	70
...	...	...	...	...	2 0	...	7 4	...	...	...	...	1 0	1 0	...	...	1 0	2 0	...	...	...	...	34	24	10	29.4	11	71
...	...	...	...	...	...	...	...	...	...	1 0	...	...	...	...	...	...	...	...	...	...	...	3	3	0	0.0	3	72
...	...	...	...	...	...	...	1 0	...	...	...	...	...	...	...	...	...	...	...	...	...	...	1	1	0	0.0	1	73
...	...	...	...	...	...	...	0 7	...	...	...	...	...	...	...	...	...	2 0	...	...	...	...	17	7	10	58.8	5	74
...	...	...	...	...	...	...	0 1	...	...	0 1	...	...	...	...	...	...	...	...	...	...	...	9	4	5	55.6	5	75
...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	1	1	0	0.0	1	76
...	...	...	...	...	5 1	...	0 1	...	...	3 1	...	...	...	...	...	1 0	1 0	...	...	...	...	25	19	6	24.0	11	77
...	...	...	...	1 0	...	...	1 0	...	...	...	...	1 0	...	...	...	...	1 0	...	...	...	...	9	7	2	22.0	8	78
...	1 0	...	...	...	1 0	...	0 1	...	...	2 0	...	1 0	...	...	...	...	4 0	...	...	...	...	18	15	3	16.7	10	79
...	1 0	...	...	...	5 2	...	5 3	...	...	2 3	...	1 0	...	...	...	...	...	...	...	0 1	...	49	32	17	34.7	14	80
...	1 0	...	...	...	...	...	...	...	...	1 0	...	...	...	...	...	...	...	...	...	...	...	5	4	1	20.0	4	81
...	...	...	...	...	0 1	...	...	...	...	...	...	...	...	...	...	...	2 0	...	...	...	...	13	9	4	30.8	8	82
...	...	...	...	...	...	...	...	...	...	1 0	...	...	...	...	...	...	...	...	...	...	...	1	1	0	0.0	1	83
...	...	...	...	...	...	...	2 1	...	...	0 1	...	...	...	...	...	...	...	...	...	...	...	6	3	3	50.0	4	84
...	1 0	...	...	...	1 0	...	...	...	...	1 0	...	...	...	1 0	...	...	2 0	...	1 0	...	...	14	12	2	14.3	9	85
...	...	...	...	0 1	7 3	...	3 3	...	...	6 4	...	2 0	...	...	...	1 0	1 0	2 2	...	...	...	70	38	32	45.7	18	86
...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	1 1	...	...	...	...	2	1	1	50.0	1	87
...	...	...	...	...	1 0	...	...	...	...	3 3	...	...	...	...	...	...	1 0	...	...	...	...	20	11	9	45.0	7	88
...	1 0	...	...	...	...	...	1 2	...	...	...	...	1 0	...	...	...	...	2 0	...	...	...	...	9	6	3	33.3	5	89
...	...	...	...	...	...	...	0 1	1 0	...	2 0	...	1 0	...	1 0	...	...	2 0	...	...	...	...	22	17	5	22.7	11	90
...	...	...	...	...	...	...	1 0	...	...	0 1	...	...	...	...	...	...	...	...	...	...	...	8	6	2	25.0	5	91
...	...	...	...	...	...	...	1 0	...	...	3 1	...	1 0	0 1	...	...	...	3 0	...	...	...	...	24	16	8	33.3	10	92
...	...	...	...	...	1 0	...	...	...	...	0 1	...	1 0	...	...	...	...	...	...	...	...	...	5	4	1	20.0	5	93
...	...	...	...	...	...	...	1 1	...	...	1 0	...	...	...	...	...	...	1 0	...	...	...	...	5	3	2	40.0	4	94
...	...	...	...	...	...	...	...	...	...	1 0	...	...	...	...	...	...	1 1	...	...	...	...	4	3	1	25.0	3	95
...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	1 0	...	...	...	...	5	4	1	20.0	4	96
...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	1 0	...	...	...	...	2	2	0	0.0	2	97
...	...	...	...	...	1 0	...	7 9	...	...	1 1	...	...	...	...	...	1 0	5 3	...	...	...	...	89	46	43	48.3	11	98
...	...	...	...	...	...	...	1 0	...	...	...	...	...	...	...	...	...	1 0	...	...	...	...	5	3	2	40.0	3	99
...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	1	0	1	100.0	1	100
...	...	...	...	...	...	...	...	...	...	0 1	...	...	...	...	...	...	...	...	...	...	1 0	6	3	3	50.0	3	101
...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	2	0	2	100.0	2	102
...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	1	1	0	0.0	1	103
...	1 0	...	...	...	...	...	10 12	...	...	3 4	...	3 0	1 2	...	...	...	8 3	1 2	...	...	...	87	57	30	34.5	16	104
...	...	...	...	...	...	...	...	...	...	...	...	2 0	...	...	...	...	...	...	...	1 0	...	7	6	1	14.3	4	105
...	...	...	...	...	0 1	...	2 2	...	...	0 1	...	...	...	...	...	...	...	...	...	...	...	9	4	5	55.6	5	106
...	...	...	...	...	...	...	3 3	...	...	...	...	...	1 0	...	...	...	...	1 1	...	...	...	15	10	5	33.3	4	107
...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	1	1	0	0.0	1	108
...	1 0	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	1 1	...	...	...	...	4	2	2	50.0	3	109
...	1 0	...	...	...	...	...	...	...	...	1 0	...	...	...	...	...	...	...	...	...	...	...	4	3	1	25.0	3	110
...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	2	2	0	0.0	2	111
...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	1	1	0	0.0	1	112
...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	1 0	...	...	...	...	...	1	1	0	0.0	1	113
...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	0 1	...	...	...	...	1	0	1	100.0	1	114
...	1 0	...	...	...	...	...	...	...	...	...	...	...	...	...	...	1 0	...	...	...	...	...	3	2	1	33.3	3	115
...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	1	1	0	0.0	1	116
...	1 0	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	0 1	...	...	...	2	1	1	50.0	2	117
...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	2	1	1	50.0	1	118
...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	1 0	...	...	...	...	1	1	0	0.0	1	119
...	...	...	...	...	2 0	...	6 1	...	...	1 0	...	...	...	...	...	...	1 0	...	...	...	...	30	20	10	33.3	11	120
19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40	41	42	43	44	45	

TABLE 29.—*Foreign Trained Physicians Ex*

Marginal Number	SCHOOL	1 Arizona		2 California		3 Colorado		4 Connecticut		5 Delaware		6 District of Columbia		7 Florida		8 Georgia		9 Hawaii		10 Illinois		11 Indiana		12 Iowa		13 Kansas		14 Maine		15 Maryland	
		P	F	P	F	P	F	P	F	P	F	P	F	P	F	P	F	P	F	P	F	P	F	P	F	P	F	P	F	P	F
	IRAQ																														
121	Royal Iraq Medical College, Bagdad			0	1															1	1										
	IRELAND																														
122	Queen's University Faculty of Medicine, Belfast							1	0																						
123	National University of Ireland			4	0			23	8											6	1							1	0	5	0
124	University of Dublin School of Physic, Trinity College, Dublin																														
125	Schools of Surgery, Royal College of Surgeons in Ireland, Dublin																														
126	Licentiate of the Royal College of Physicians of Ireland																														
127	Licentiate of the Royal College of Physicians of Ireland, Licentiate of the Royal College of Surgeons in Ireland									0	1																				
128	Licentiate of the Royal College of Surgeons, Ireland																														
	ISRAEL																														
129	Hadassah Medical School, Hebrew University, Jerusalem																			4	0										
	ITALY																														
130	Univ. degli Studi di Bologna, Facolta di Medicina e Chirurgia			1	2			1	1					1	0					4	3							2	0		
131	Univ. degli Studi di Milano, Facolta di Medicina e Chirurgia			0	1															0	1										
132	Univ. degli Studi di Catania, Facolta di Medicina e Chirurgia			1	2																							1	0		
133	Univ. degli Studi di Firenze, Facolta di Medicina e Chirurgia																														
134	Univ. degli Studi di Genova, Facolta di Medicina e Chirurgia																			3	1										
135	Univ. degli Studi di Messina, Facolta di Medicina e Chirurgia																													0	1
136	Univ. degli Studi di Modena, Facolta di " "							0	1																			0	1		
137	Univ. di Napoli, Facolta di Medicina e "	0	1	1	1			2	2											1	1									1	0
138	Univ. degli Studi di Padova, Facolta di " "																			2	0										
139	Univ. degli Studi di Palermo, Facolta di Medicina e Chirurgia							0	1											1	1										
140	Univ. degli Studi di Parma, Facolta di Medicina e Chirurgia																			1	0										
141	Univ. degli Studi di Pavia, Facolta di Medicina e Chirurgia																			1	1										
142	Univ. degli Studi di Pisa, Facolta di Medicina e Chirurgia							1	0											0	2										
143	Univ. degli Studi di Roma, Facolta di Medicina e Chirurgia			2	1			6	1											4	3	1	0							2	1
144	Univ. degli Studi di Siena, Facolta di Medicine e Chirurgia													0	1					0	1										
145	Univ. di Torino, Facolta di Medicina e Chirurgia							2	2																						
146	Universita degli Studi "Benito Mussolini" di Bari, Facolta di Medicine e Chirurgia			1	0															1	1										
147	Libera Universita degli Studi di Camerino Facolta di Medicine e Chirurgia																														
	JAPAN																														
148	Kyoto Imperial University Faculty of Medicine			1	0																										
149	Tokyo Imperial University Faculty of Medicine																													1	[illegible]
150	Tokyo Medical College, Hongo, Tokyo	1	0																												
151	Tokyo Women's Special Medical School																	1	0												
152	Keio Gijuku University Medical College, Tokyo							1	1																						
153	Teikoku Women's Medical-Pharmacological College, Tokyo																	0	1												
154	Faculty of Medicine Nihon University, Tokyo																	0	1												
155	Yamaguchi Prefectural University of Medicine																														
156	Faculty of Medicine, Hokkaido University, Sapporo, Hokkaido																														
157	Yokohama University Faculty of Medicine, Yokohama																														
158	Japan Medical College, Hongo, Tokyo																														
	KOREA																														
159	Severance Union Medical College, Seoul							0	1																						
160	College of Medicine, Seoul National University, Seoul							2	0																					1	[illegible]
161	Soo do Medical College, Seoul							0	1																						
162	Taegu Medical College, Kyong Puk University, Taegu																													1	[illegible]
163	Pyung Yang Medical College, Pyung Yang																					1	0								
	LATVIA																														
164	Latvijas Universitate Medicinas Fakultate, Riga																			0	2							0	1		
	LEBANON																														
165	American University of Beirut School of Medicine			2	0							1	0							2	0			1	0					1	[illegible]
166	Faculte Francaise de Medecine de l'Universite de St. Joseph, Beyrouth			2	0			1	3											1	0	1	0								
	LITHUANIA																														
167	Vytauto Didziojo Universeto Medicinos Fakulteto, Kaunas																			5	3										
	MALTA																														
168	University of Malta Faculty of Medicine and Surgery																														
	MEXICO																														
169	Universidad Nacional Autonoma de Mexico Facultad de Medicina, Mexico, D.F.	1	0	6	2			3	0							1	0			19	14									1	1
170	Escuela de Medicina de Nuevo Leon, Monterrey			0	2															1	3										
171	Universidad de Guadalajara Facultad de Ciencias Medicas y Biologicas																	1	0	0	4										
172	Instituto Literario y Cientifico, San Luis Potosi							0	1																						
173	Facultad de Medicina de la Universidad Nacional del Sureste, Merida, Yucatan			1	0															1	0					1	0				
174	Escuela Libre de Homeopatia, Mexico, D.F.																														
175	Universidad Autonoma Facultad de Medicina, Guadalajara																														
176	Escuela Nacional de Medicina Homeopatico del Instituto Politecnico Nacional, Mexico, D.F.																														
	NETHERLANDS																														
177	Universiteit van Amsterdam Geneeskunde Faculteit			0	1			1	0									2	0	1	0									2	1
178	Rijks-Universiteit te Groningen Medische Faculteit			1	0																							1	0		
179	Rijks-Universiteit te Leiden Faculteit der Geneeskunde			1	0	1	0	3	1					2	0	2	0			4	1										
180	Rijks-Universiteit te Utrecht Faculteit der Geneeskunde			1	0			2	1											1	0										
	NICARAGUA																														
181	Universidad de Nicaragua Facultades de Medicina en Leon y en Granada			1	1															1	2									1	0
	NORWAY																														
182	Kongelige Frederiks Universitet Medisinske Fakultet, Oslo																														
	PAKISTAN																														
183	King Edward Medical College, Lahore, Punjab																														
Marginal Number		1		2		3		4		5		6		7		8		9		10		11		12		13		14		15	

P—Passed; F—Failed

19 Mississippi		20 Missouri		21 Montana		22 Nebraska		23 New Hampshire		24 New Jersey		25 New Mexico		26 New York		27 North Carolina		28 North Dakota		29 Ohio		30 Oregon		31 Pennsylvania		32 Rhode Island		33 South Dakota		34 Tennessee		35 Texas		36 Virginia		37 Washington		38 West Virginia		39 Wisconsin		40 Canal Zone, Guam, Puerto Rico, Virgin Islands		41 Totals	42 Examined—Passed	43 Examined—Failed	44 Percentage Failed	45 Number of Boards Examined by	Marginal Number
P	F	P	F	P	F	P	F	P	F	P	F	P	F	P	F	P	F	P	F	P	F	P	F	P	F	P	F	P	F	P	F	P	F	P	F	P	F	P	F	P	F	P	F						
																																		1	1									6	3	3	50.0	4	121
														1	0									1	0									1	0									4	4	0	0.0	4	122
		3	0							3	0			5	1							1	0	1	0							1	0	1	0	0	1							72	58	14	19.4	15	123
										1	0															2	1																	5	4	1	20.0	3	124
		1	0																																									1	1	0	0.0	1	125
										1	0															0	1																	3	2	1	33.3	3	126
																				1	0													1	0									3	2	1	33.3	3	127
														1	0																													1	1	0	0.0	1	128
														1	0											1	0																	6	6	0	0.0	3	129
										17	1			22	22					1	2			1	0	6	1							2	0									94	61	33	35.1	12	130
														0	3					1	0			1	0																			7	2	5	71.4	5	131
														1	2																													7	3	4	57.1	3	132
										1	0			1	0																									1	0			5	5	0	0.0	5	133
										1	0			3	2																													10	7	3	30.0	3	134
										1	0			0	2					2	1			1	0									0	1									9	4	5	55.6	6	135
										1	1			0	1					0	1																							6	1	5	83.3	5	136
										5	3			12	15					1	2													1	1									52	25	27	51.9	10	137
										4	1			9	5																			0	2									24	15	9	37.5	5	138
										2	2			6	7					0	2			1	0									1	0									24	11	13	54.2	7	139
																																												1	1	0	0.0	1	140
										1	0			1	0																													4	3	1	25.0	3	141
														2	0									1	0																			6	4	2	33.3	4	142
		1	0							17	4			28	21					2	2			5	0	1	0							5	0					1	0			109	76	33	30.3	14	143
																																												2	0	2	100.0	2	144
										2	0			7	4					0	1																							18	11	7	38.9	4	145
														2	2																													7	4	3	42.9	3	146
																				1	0																							1	1	0	0.0	1	147
																																												1	1	0	0.0	1	148
																																												2	1	1	50.0	1	149
																																												1	1	0	0.0	1	150
																																												2	2	0	0.0	2	151
														0	1																			0	1									4	1	3	75.0	3	152
																																												1	0	1	100.0	1	153
																																												1	0	1	100.0	1	154
																																		1	1									2	1	1	50.0	1	155
																																		1	0									1	1	0	0.0	1	156
																																		1	0									1	1	0	0.0	1	157
																				1	0																							1	1	0	0.0	1	158
																																		4	0									6	5	1	16.7	3	159
																																												4	3	1	25.0	3	160
																										0	1							1	0									3	1	2	66.7	3	161
																																												1	1	0	0.0	1	162
																																												1	1	0	0.0	1	163
														0	7					1	3																							14	1	13	92.8	4	164
1	0	1	0											4	1									2	0							2	1	3	2									25	21	4	16.0	12	165
																								1	0	0	1																	12	7	5	41.7	7	166
										1	0			2	7					1	3																							23	10	13	56.5	5	167
														1	0																													1	1	0	0.0	1	168
										1	1			1	0					3	2			1	0							5	3	5	1			1	0	1	0	24	5	103	73	30	29.1	16	169
																																7	4	0	1	1	0							19	9	10	52.6	5	170
																																										1	0	6	2	4	66.7	3	171
																																												1	0	1	100.0	1	172
																																												2	2	0	0.0	2	173
																																										1	0	2	2	0	0.0	2	174
																																												1	0	1	100.0	1	175
																																		2	1									3	2	1	33.3	1	176
				1	0	1	0			3	0			8	0			1	0					5	0									1	0	1	0							30	28	2	6.7	14	177
		1	0					1	0	2	0			2	0					1	0			1	0																			10	10	0	0.0	8	178
										3	0	1	0	11	6					1	0							1	0			1	0	2	0	4	2							52	41	11	21.2	16	179
										2	0			2	0					3	0			1	0			1	0					1	0	2	0							17	16	1	5.9	10	180
																		1	0																									7	4	3	42.9	4	181
						1	0																																					2	2	0	0.0	2	182
1	0	2	0																																									3	3	0	0.0	2	183

TABLE 29.—*Foreign Trained Physicians Exa*

Marginal Number	SCHOOL	1 Arizona		2 California		3 Colorado		4 Connecticut		5 Delaware		6 District of Columbia		7 Florida		8 Georgia		9 Hawaii		10 Illinois		11 Indiana		12 Iowa		13 Kansas		14 Maine		15 Maryland		16 Massachusetts	
		P	F	P	F	P	F	P	F	P	F	P	F	P	F	P	F	P	F	P	F	P	F	P	F	P	F	P	F	P	F	P	F
	PARAGUAY																																
181	National University of Paraguay Faculty of Medical Sciences, Asuncion			0	1																												
	PERU																																
185	Universidad Mayor de San Marcos de Lima Facultad de Medicina			1	0															1	1									1	0		
	PHILIPPINES																																
186	University of Santo Tomas Faculty of Medicine and Surgery, Manila			4	7			1	1									0	1	10	3	2	1							1	1	1	[illegible]
187	University of the Philippines College of Medicine, Manila			1	0			1	0											2	0												
188	Afable College of Medicine, Manila			0	1																												
189	Centro Medical College, Manila			1	0																												
190	Manila Central University, College of Medicine, Manila																			0	3									1	0		
	POLAND																																
191	Uniwersytet Jagiellonski Wydzial Lekarski, Cracow																			1	1												
192	Uniwersytet Jana Kazimierza Wydzial Lekarski, Lwow							0	1											0	2									1	0		
193	Uniwersytet Jozefa Pilsudskiego, Warszawa			0	1															1	1												
194	Uniwersytet Poznanski Wydzial Lekarski, Poznan																			1	1												
195	Uniwersytet Stefano Batorego Wydzial Lekarski, Wilno																																
	PORTUGAL																																
196	Universidade de Coimbra Faculdade de Medicina							1	0											0	1												
197	Universidade de Lisbon *Faculdade de Medicina*							1	0																					1	0	0	1
198	Universidade de Porto Faculdade de Medicina																																
	RUMANIA																																
199	Universitatea din Bucuresti Facultatea de Medicina																																
200	Universitatea Regele Ferdinand I-iu din Cluj Facultatea de Medicina si Farmacie																			1	0												
201	Universitatea din Iasi Facultatea de Medicina																			0	1												
	SCOTLAND																																
202	University of Aberdeen Faculty of Medicine																			1	1												
203	University of St. Andrews Conjoint Medical School, St. Andrews and Dundee																																
204	University of Edinburgh Faculty of Medicine																									1	0						
205	University of Glasgow Medical Faculty	1	0	1	0							2	0																	2	0	0	1
206	*Licentiate of the Royal Colleges of Physicians and Surgeons of Edinburgh, Licentiate of the Royal Faculty of Physicians and Surgeons of Glasgow*	1	0											1	1											1	0					1	0
207	Polish School of Medicine, Edinburgh																																
208	*Licentiate of the Royal College of Physicians of Edinburgh*																																
	SOUTH AFRICA																																
209	University of the Witwatersrand Medical School, Johannesburg																			1	0											1	0
210	University of Cape Town Faculty of *Medicine, Cape Town*																															2	0
	SPAIN																																
211	Universidad de Barcelona Facultad de Medicina			1	0															1	0												
212	Universidad de Sevilla Facultad de Medicina																													1	0		
213	Universidad de Granada Facultad de Medicina																			2	1												
214	Universidad Central de Espana Facultad de Medicina, Madrid			0	1									2	0					2	1									0	1		
215	*Universidad de Santiago Facultad de Medicina*																			1	0												
216	Universidad de Zaragoza Facultad de Medicina																			1	0												
217	Universidad de Valencia Facultad de Medicina							1	0											0	2												
218	Universidad Literaria de Valladolid Facultad de Medicina																			1	0												
219	*Universidad de Salamanca Facultad de Medicina*																																
	SWEDEN																																
220	Karolinska Mediko-Kirurgiska Institutet, Stockholm																																
221	Kungl, Karolinska Universitetet Medicinska Fakulteten, Lund																															0	1
	SWITZERLAND																																
222	Universitat Basel Medizinische Fakultat			1	0			1	0			1	0							0	1												
223	Universitat Bern Medizinische Fakultat			1	0			2	1					2	0					3	0												
224	Universite de Geneve Faculte de Medecine							6	3			4	0	5	1	3	0			1	0									1	0	1	0
225	Universite de Lausanne Faculte de Medecine			1	2			7	2					2	1					2	0									1	0		
226	Universitat Zurich Medizinische Fakultat			1	1			4	0					2	2			2	0	2	0											2	1
	THAILAND																																
227	Chulakankarana University Faculty of Medicine, Bangkok																																
	TURKEY																																
228	University of Istanbul Medical Faculty			1	0			4	2											4	7	1	0							2	0		
229	Ankara University Faculty of Medicine			0	1			2	0																								
	UNION OF SOCIALIST SOVIET REPUBLICS																																
230	*First Leningrad Medical Institute, Leningrad*																																
231	Kazan Medical Institute, Kazan																																
232	Kharkov Medical Institute, Kharkov																			0	1												
233	Kiev Medical Institute, Kiev																			1	2												
234	First Moscow Medical Institute																			1	2												
235	Severo-Kavka Medical Institute, Rostov-on-the-Don																																
236	Krim Medical Institute,																			1	1												
237	Kuban Red Army Institu																																
238	Tbilisi Institute of Medicine, Tbilisi																			1	0												
239	Stalino Institute of Medicine, Stalino																			1	1												
240	Ashkhabad Institute of Medicine, Ashkhabad																																
241	Daghestan Medical Institute, Makhach, Kala																																
	URUGUAY																																
242	Universidad de Montevideo Facultad de Medicine							1	0																								
	YUGOSLAVIA																																
243	Zagrebaskog Universiteta Medecinski Fakultet, Zagreb			1	0															6	0									1	0		
244	Beogradskog Universiteta Medecinski Fakultet, Beograd			0	1															3	3												
	Totals Examined—Passed	7		85		2		136		1		14		32		19		9		345		15		1		9		19		51		[illegible]	
	Totals Examined—Failed	2		54		0		76		1		0		10		2		3		229		2		0		0		5		12		[illegible]	
	Totals	9		139		2		212		2		14		42		21		12		574		17		1		9		24		63		[illegible]	
	Percentage Failed	22.2		38.8		0.0		35.8		50.0		0.0		23.8		9.5		33.3		39.8		11.8		0.0		0.0		20.8		19.0		[illegible]	
	Marginal Number	1		2		3		4		5		6		7		8		9		10		11		12		13		14		15		16	

P—Passed; F—Failed

19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40	41	42	43	44	45	
Mississippi	Missouri	Montana	Nebraska	New Hampshire	New Jersey	New Mexico	New York	North Carolina	North Dakota	Ohio	Oregon	Pennsylvania	Rhode Island	South Dakota	Tennessee	Texas	Virginia	Washington	West Virginia	Wisconsin	Canal Zone, Guam, Puerto Rico, Virgin Islands	Totals	Examined—Passed	Examined—Failed	Percentage Failed	Number of Boards Examined by	Marginal Number
P F	P F	P F	P F	P F	P F	P F	P F	P F	P F	P F	P F	P F	P F	P F	P F	P F	P F	P F	P F	P F	P F						
																						1	0	1	100.0	1	184
					1 0		0 1															6	4	2	33.3	5	185
	3 0									2 0		1 0					7 4				1 0	54	33	21	38.9	12	186
							6 2			2 0						1 1						16	13	3	18.7	6	187
																						1	0	1	100.0	1	188
																						1	1	0	0.0	1	189
	1 0									2 0										1 0		8	5	3	37.5	5	190
							1 4															7	2	5	71.4	2	191
					1 1		1 2			0 1							1 0					11	4	7	63.6	7	192
					1 1		6 3						1 0									15	9	6	40.0	5	193
					1 0		0 1		1 0	1 0												6	4	2	33.3	5	194
							1 2			0 1												4	1	3	75.0	2	195
													1 0									3	2	1	33.3	3	196
																	1 0					4	3	1	25.0	4	197
																		1 0				1	1	0	0.0	1	198
							0 1										1 0					2	1	1	50.0	2	199
							1 1			1 0												5	4	1	20.0	4	200
																						1	0	1	100.0	1	201
												2 0										4	3	1	25.0	2	202
							1 0															1	1	0	0.0	1	203
							1 0						1 0			1 0						5	5	0	0.0	5	204
							2 0									1 1	1 0					12	10	2	16.7	8	205
							0 1					1 0										7	5	2	28.6	6	206
					0 2		0 1															3	0	3	100.0	2	207
																		1 0				1	1	0	0.0	1	208
							2 1															5	4	1	20.0	3	209
							3 0					1 0										6	6	0	0.0	3	210
										1 0											5 0	8	8	0	0.0	4	211
																						1	1	0	0.0	1	212
																	1 1				1 0	6	4	2	33.3	3	213
	1 0				1 0		1 0			1 0							2 1			1 0	51 2	67	62	5	7.5	11	214
							0 1														11 2	13	12	1	7.7	3	215
																	1 0				2 0	5	5	0	0.0	4	216
						1 1						1 0					1 0					7	4	3	42.9	5	217
																					3 0	4	4	0	0.0	2	218
																					5 0	5	5	0	0.0	1	219
																		1 0				1	1	0	0.0	1	220
																						1	0	1	100.0	1	221
	1 0				5 0		7 7			1 2							0 1			1 0		29	18	11	37.9	10	222
					4 0		2 0			1 0		1 0				1 0		0 1				19	17	2	10.5	10	223
0	1 0				6 0		27 12	1 0		1 0						1 0				2 0		77	61	16	20.8	15	224
	1 0				4 0		12 7			2 0		4 0				1 0	0 1					50	37	13	26.0	12	225
					4 0		6 2					2 0	1 0			1 0				0 1		35	28	7	20.0	13	226
																1 0						1	1	0	0.0	1	227
					1 0		4 3					1 0					3 5					40	23	17	42.5	11	228
					1 1		0 1										2 1					9	5	4	44.4	5	229
					0 1																	1	0	1	100.0	1	230
							0 1															1	0	1	100.0	1	231
					0 1																	2	0	2	100.0	2	232
					1 0					0 3		1 0										9	4	5	55.6	5	233
					1 0		0 1			0 1												6	2	4	66.7	4	234
										0 1												1	0	1	100.0	1	235
																						2	1	1	50.0	1	236
										0 1												1	0	1	100.0	1	237
										0 1												2	1	1	50.0	2	238
																						2	1	1	50.0	1	239
										1 0		1 0										2	2	0	0.0	2	240
										0 1												1	0	1	100.0	1	241
																1 0	0 1					3	2	1	33.3	3	242
							3 4															14	10	4	28.6	3	243
							1 2			2 2							1 0					16	8	8	50.0	6	244
	36	1	3	2	136	2	343	2	3	90	1	72	25	7	1	40	122	18	4	13	116	1,870					
	0	0	0	1	33	0	270	0	0	67	0	0	9	1	0	12	45	17	0	2	10	896					
	36	1	3	3	169	2	613	2	3	157	1	72	34	8	1	52	167	35	4	15	126	2,766					
	0.0	0.0	0.0	33.3	19.5	0.0	44.0	0.0	0.0	42.7	0.0	0.0	26.5	12.5	0.0	23.1	26.9	48.6	0.0	13.3	7.9	32.4					
	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40	41	42	43	44	45	

BOARDS OF EXAMINERS IN THE BASIC SCIENCES

Twenty-one states and the District of Columbia have adopted basic science requirements as a prerequisite for licensure. The law in most of these applies to any person practicing the healing arts or any branch thereof, whereas the law in a few states indicates that it specifically applies to those persons planning to engage in the practice of medicine, osteopathy, and chiropractic; still others include the practice of naturopathy, chiropody, and dentistry.

CORRESPONDING OFFICERS OF BOARDS OF MEDICAL EXAMINERS IN THE UNITED STATES, TERRITORIES, AND OUTLYING POSSESSIONS

Alabama	Dr. D. G. Gill, Secretary, State Office Bldg., Montgomery 4.
Alaska	Dr. W. M. Whitehead, Secretary, 172 S. Franklin St., Juneau.
Arizona	Mr. Robert Carpenter, Executive Secretary, 1021 Central Towers North, 2727 N. Central Ave., Phoenix.
Arkansas	Dr. Joe Verser, Secretary, Harrisburg.
California	Dr. Louis E. Jones, Secretary, Room A-547, 1021 O St., Sacramento.
Canal Zone	Dr. Eric R. Osterberg, Health Director, Balboa Heights.
Colorado	Dr. John B. Farley, Secretary, 715 Republic Bldg., 1612 Tremont Pl., Denver 2.
Connecticut	Dr. Stanley B. Weld, Secretary, 160 St. Ronan St., New Haven.
Delaware	Dr. Joseph S. McDaniel, Secretary, Professional Bldg., Dover.
District of Columbia	Mr. Paul Foley, Deputy Director, 1740 Massachusetts Ave., N. W., Washington.
Florida	Dr. Homer L. Pearson, Secretary, 901 N. W. 17th St., Miami 36.
Georgia	Mr. Cecil L. Clifton, Secretary, 224 State Capitol, Atlanta 3.
Guam	Dr. John E. Kennedy, Secretary, Marianos Islands, Agana.
Hawaii	Dr. R. Allen Richardson, Chairman, 1000 Ward Ave., Honolulu.
Idaho	Mr. Armand L. Bird, Executive Secretary, 358 Sonna Bldg., Boise.
Illinois	Mr. Fredric B. Selcke, Superintendent of Registration, Capitol Bldg., Springfield.
Indiana	Miss Ruth V. Kirk, Executive Secretary, 538 K. of P. Bldg., Indianapolis.
Iowa	Mr. Ronald V. Saf, Executive Secretary, 510 Empire Bldg., Des Moines 9.
Kansas	Dr. F. J. Nash, Secretary, New Brotherhood Bldg., Kansas City.
Kentucky	Dr. Russell E. Teague, Secretary, 620 S. Third St., Louisville 2.
Louisiana	Dr. Edwin H. Lawson, Secretary, 930 Hibernia Bank Bldg., New Orleans 12.
Maine	Dr. Daniel F. Hanley, Secretary, Box 637, Brunswick.
Maryland	Dr. Frank K. Morris, Secretary-Treasurer, 1211 Cathedral St., Baltimore 1.
Massachusetts	Dr. David W. Wallwork, Secretary, State House, Room 37, Boston 33.
Michigan	Dr. E. C. Swanson, Executive Secretary, 118 Stevens T. Mason Bldg., W. Michigan Ave., Lansing 8.
Minnesota	Dr. F. H. Magney, Secretary, 230 Lowry Medical Arts Bldg., St. Paul 2.
Mississippi	Dr. A. L. Gray, Executive Officer, Old Capitol, Jackson 13.
Missouri	Mr. John A. Hailey, Executive Secretary, State Capitol Bldg., P. O. Box 4, Jefferson City.
Montana	Dr. Thomas L. Hawkins, Secretary, 555 Fuller Ave., Helena.
Nebraska	Mr. R. K. Kirkman, Director, Room 1009, State Capitol Bldg., Lincoln 9.
Nevada	Dr. George H. Ross, Secretary, 112 N. Curry St., Carson City.
New Hampshire	Dr. Edward W. Colby, Secretary, 61 S. Spring St., Concord.
New Jersey	Dr. Royal A. Schaaf, Secretary, 28 W. State St., Trenton.
New Mexico	Dr. R. C. Derbyshire, Secretary, 227 E. Palace Ave., Santa Fe.
New York	Dr. Stiles D. Ezell, Secretary, 23 S. Pearl St., Albany 7.
North Carolina	Dr. Joseph J. Combs, Secretary, 716 Professional Bldg., Raleigh.
North Dakota	Dr. C. J. Glaspel, Secretary, Box 228, Grafton.
Ohio	Dr. H. M. Platter, Secretary, 21 W. Broad St., Columbus 15.
Oklahoma	Dr. E. F. Lester, Secretary, 813 Braniff Bldg., Oklahoma City.
Oregon	Mr. Howard I. Bobbitt, Executive Secretary, 609 Failing Bldg., Portland 4.
Pennsylvania	Mrs. Margaret G. Steiner, Secretary, Box 911, Harrisburg.
Puerto Rico	Mr. Herminie Mendez Herrera, Acting Secretary, Box 9156, Santurce.
Rhode Island	Mr. Thomas B. Casey, Administrator, 366 State Office Bldg., Providence.
South Carolina	Dr. Harold E. Jervey, Jr., Secretary, 1329 Blanding St., Columbia.
South Dakota	Mr. John C. Foster, Executive Secretary, 300 First National Bank Bldg., Sioux Falls.
Tennessee	Dr. Alfred H. Mason, Secretary, 1635 Exchange Bldg., Memphis 3.
Texas	Dr. M. H. Crabb, Secretary, 1714 Medical Arts Bldg., Forth Worth 2.
Utah	Mr. Frank E. Lees, Director, 324 State Capitol Bldg., Salt Lake City 1.
Vermont	Dr. F. J. Lawliss, Secretary, Richford.
Virgin Islands	Dr. Benjamin A. Nath, Secretary, Charlotte Amalie, St. Thomas.
Virginia	Dr. K. D. Graves, Secretary, 631 First St., S. W., Roanoke.
Washington	Mr. Thomas A. Carter, Administrator, Capitol Bldg., Olympia.
West Virginia	Dr. Newman H. Dyer, Secretary, State Office Bldg., No. 3, Charleston 5.
Wisconsin	Dr. Thomas W. Tormey, Jr., Secretary, 115 S. Pinckney St., Madison.
Wyoming	Dr. Carleton D. Anton, Acting Secretary, State Office Bldg., Cheyenne.

A basic science law provides for the establishment of a board of examiners and requires that each person to whom the law applies appear before the board and demonstrate his knowledge of the basic sciences. These boards have no licensing powers. A certificate of proficiency in fundamental sciences is issued which must be presented when applying for a license to practice medicine or other method of healing. The function of the basic science board in the District of Columbia is to examine all applicants referred to it by the Commission on Licensure and does not issue any type of certificate.

The states comprising this group, together with the year of enactment of the basic science law for each, are included in table 34. This table presents, in composite form, the subjects in which examinations are given by each board and the interstate registration policies for certification without examination (i. e., by reciprocity, waiver or exemption). All boards examine in anatomy, pathology, and physiology; 20, in bacteriology and chemistry; 10, in hygiene; 2, in diagnosis; and 1, in public health. The first state to enact this form of legislation was Wisconsin, in 1925. Kansas, under a "Healing Arts Act" in 1957, was the last state to require such certification. The Arkansas Basic Science Board was abolished by legislative action in 1959 and was replaced by the State Healing Arts Board. The first examination was given by this board in April, 1959. A basic science law was enacted in Alabama in 1959, and the board will give its first examination in June, 1960.

TABLE 30.—*Physicians Examined on the Basis of Credentials Obtained in Countries Other Than the United States and Canada, 1930-1959*

Year	Number Examined	Passed	Percentage Failed
1930	167	92	44.9
1931	158	91	42.4
1932	182	96	17.3
1933	200	129	35.5
1934	285	170	40.2
1935	437	303	30.7
1936	588	382	35.0
1937	920	637	30.8
1938	1,164	716	38.5
1939	1,691	839	50.4
1940	2,088	948	54.7
1941	1,717	698	59.2
1942	1,630	890	45.4
1943	1,031	518	49.8
1944	691	325	53.0
1945	475	209	56.0
1946	495	221	55.3
1947	601	283	52.9
1948	639	311	51.3
1949	737	319	56.7
1950	799	359	55.0
1951	1,006	524	47.9
1952	1,208	648	46.3
1953	1,463	796	46.3
1954	1,642	943	42.6
1955	1,771	1,042	41.4
1956	1,783	1,012	43.2
1957	2,299	1,345	41.5
1958	2,567	1,518	40.9
1959	2,766	1,870	32.4
Totals	33,200	18,234	45.1

The results of examinations given and the number of certificates issued on the basis of reciprocity, endorsement, waiver, or exemption, during 1959, are presented in tables 35 and 36. A candidate, in applying for a basic science certificate, is not required by law to reveal his school of practice. No attempt has been made to differentiate the schools of the healing arts represented by the candidates examined or certified. For two states, the failure data was not reported. The percentage of candidates failing the basic science examination is given for those states that did submit these data.

There were 4,583 candidates examined by the 22 boards in operation in 1959, and certificates of proficiency were issued to 3,315 individuals after written examination. In addition, as noted in table 36, there were 2,680 certificates issued without examination by 20 boards. The number of applicants registered, with or without written examination, in 1959, was 5,996. Texas issued 745 such certificates; Michigan, 695; Florida, 658; Minnesota, 448; and Washington, 420. Other states certified fewer than 400. In Florida, the 658 certificates issued were by written examination; this state does not have reciprocal or waiver privileges.

Table 37 records the number of candidates certified by basic science boards since 1927. This table indicates for each year the number of boards in operation, the number of candidates who passed and failed, the number registered without written examination, and the total certified. In this 33-year period, 101,064 certificates have been issued by boards in the basic sciences, 69,597 by examination, and 32,467 by reciprocity, endorsement, exemption, or waiver. The percentage of failures in the examination during this 33-year period was 20.9.

The registration or examination fee in the states requiring basic science certification is given in table 38. In seven instances, a higher fee is exacted of those desiring certification without written examination. Examination and endorsement meetings are held in most instances semiannually or coincide with the examination and meetings scheduled by the licensing boards. The JOURNAL publishes biweekly the future dates of examination and reciprocity or waiver meetings of all basic science boards.

In 1959, there were 4,583 examinations given by basic science boards; 3,315 were successful, and 1,268 examination results were reported as unsuccessful. Unless permitted reexamination, the latter group does not qualify for consideration for licensure in the healing art in which they are interested. The several basic science boards differ widely from each other in the restrictions put upon the candidate with respect to repetition of examinations that have been failed and the accumulation of credit. Because of these differences, the data in this section are presented in factual form as reported; no attempt has been made to analyze the data on a comparable basis from state to state.

While the informative data presented may be useful to those seeking licensure in these states, it is recommended that the information be supplemented by direct communication with the basic science board. The present executive corresponding officer of each of the 22 basic science boards is as follows:

Alaska..........Dr. R. Harrison Leer, Box 204, Alaska Office Bldg., Juneau.
Arizona..........Mr. Herman E. Bateman, University of Arizona, Tucson.
Arkansas..........Dr. A. W. Ford, State Healing Arts Board, Dept. of Education, Education Bldg., Little Rock.
Colorado..........Dr. Esther B. Starks, 1459 Ogden St., Denver 18.
Connecticut..........Mrs. Regina G. Brown, State Board of Healing Arts, 258 Bradley St., New Haven 10.
District of Columbia..Mr. Paul Foley, Commission on Licensure, 1740 Massachusetts Ave., N. W., Washington 6.
Florida..........Mr. M. W. Emmel, University of Florida, Box 340, Gainesville.
Iowa..........Dr. Elmer W. Hertel, Waverly.
Kansas..........Dr. Leon C. Heckert, Kansas State College, Pittsburg.
Michigan..........Mrs. Anne Baker, 116 Stevens T. Mason Bldg., W. Michigan Ave., Lansing.
Minnesota..........Dr. Raymond N. Bieter, 105 Millard Hall, University of Minnesota, Minneapolis 14.

TABLE 31.—*Foreign-Trained Physicians Licensed By State Boards, 1946-1959*

	Examination							Reciprocity and Endorsement							Grand Total
	1946-1954	1955	1956	1957	1958	1959	Total	1946-1954	1955	1956	1957	1958	1959	Total	
Alabama	6	1	1	1	2	0	11	3	0	0	1	0	2	6	17
Alaska	0	0	0	0	1	0	1	0	0	0	0	0	0	0	1
Arizona	3	2	2	6	3	7	23	5	4	1	0	0	0	10	33
Arkansas	1	0	0	0	0	0	1	1	1	0	0	0	0	2	3
California	467	135	129	90	98	85	1,004	50	0	0	0	0	0	50	1,054
Colorado	41	3	0	4	1	2	51	0	0	0	0	0	0	0	51
Connecticut	81	13	25	87	136	136	478	96	23	16	19	5	4	163	641
Delaware	5	1	3	4	3	1	17	8	0	0	1	2	0	11	28
District of Columbia	33	2	2	8	15	14	74	72	10	12	16	26	32	168	242
Florida	73	27	14	28	14	32	188	0	0	0	0	0	0	0	188
Georgia	25	2	5	5	8	19	64	10	3	6	2	1	8	30	94
Hawaii	0	0	0	0	0	9	9	0	0	0	0	0	0	0	9
Idaho	0	0	0	1	0	0	1	0	0	0	0	0	0	0	1
Illinois	811	157	79	128	160	345	1,680	3	0	0	0	0	0	3	1,683
Indiana	23	2	3	6	8	15	57	23	4	9	21	17	28	102	159
Iowa	22	4	12	7	2	1	48	32	1	1	3	1	9	47	95
Kansas	6	3	5	2	1	9	26	0	0	0	0	0	0	0	26
Kentucky	1	0	0	0	0	0	1	3	0	1	0	0	1	5	6
Louisiana	4	1	0	0	1	0	6	0	0	0	0	0	0	0	6
Maine	47	41	25	24	26	19	182	19	6	4	5	8	10	52	234
Maryland	178	55	71	126	114	51	595	7	0	1	1	0	0	9	604
Massachusetts	65	11	16	24	21	42	179	13	2	4	0	0	0	19	198
Michigan	56	40	23	30	31	33	213	18	17	14	23	14	13	99	312
Minnesota	67	17	16	17	14	10	141	0	0	0	1	0	0	1	142
Mississippi	8	2	0	2	5	3	20	2	0	0	0	0	0	2	22
Missouri	43	14	11	9	2	36	115	6	0	2	0	0	0	8	123
Montana	1	0	0	0	0	1	2	3	0	0	0	0	1	4	6
Nebraska	3	0	1	1	1	3	9	8	0	0	1	3	1	13	22
Nevada	0	0	0	0	1	0	1	1	0	0	0	0	0	1	2
New Hampshire	12	3	6	5	1	2	29	26	3	5	7	7	5	53	82
New Jersey	60	23	41	86	111	136	457	219	22	42	23	37	22	365	822
New Mexico	5	4	0	3	2	2	16	17	1	2	0	0	0	20	36
New York	1,441	159	193	268	352	343	2,756	255	7	5	1	3	5	276	3,032
North Carolina	30	0	0	1	1	2	34	6	2	1	1	1	2	13	47
North Dakota	25	5	7	2	1	3	43	0	0	0	0	0	0	0	43
Ohio	308	160	117	86	71	90	832	236	47	27	19	71	94	494	1,326
Oklahoma	2	0	0	0	0	0	2	4	1	0	0	1	2	8	10
Oregon	1	0	0	0	1	1	3	0	0	0	0	0	0	0	3
Pennsylvania	54	6	10	15	35	72	192	0	0	0	0	0	0	0	192
Rhode Island	103	35	39	36	42	25	280	3	1	2	4	11	0	21	301
South Carolina	1	0	0	0	0	0	1	0	0	0	0	0	0	0	1
South Dakota	20	4	1	13	1	7	46	1	0	1	3	0	2	7	53
Tennessee	7	0	2	0	0	1	10	3	0	3	0	5	5	16	26
Texas	64	16	17	34	35	40	206	28	3	4	1	3	7	46	252
Vermont	1	0	0	0	0	0	1	5	3	2	2	2	0	14	15
Virginia	62	54	84	91	95	122	508	16	0	0	0	0	0	16	524
Washington	26	5	7	9	12	18	77	17	6	5	7	17	24	76	153
West Virginia	10	0	8	7	4	4	33	0	0	0	0	0	0	0	33
Wisconsin	9	2	2	7	14	13	47	7	1	8	13	10	12	51	98
Wyoming	0	0	0	0	1	0	1	2	0	0	0	0	0	2	3
U. S. Possessions and Territories	92	30	35	72	71	116	416	27	0	2	5	5	0	39	455
Totals	4,400	1,042	1,012	1,345	1,518	1,870	11,187	1,255	168	180	180	250	289	2,322	13,509

Nebraska	Mr. R. K. Kirkman, Room 1009, State Capitol Bldg., Lincoln 9.
Nevada	Dr. Kenneth C. Kemp, University of Nevada, Reno.
New Mexico	Mrs. Marguerite Cantrell, Box 1522, Santa Fe.
Oklahoma	Dr. E. F. Lester, 813 Braniff Bldg., Oklahoma City.
Oregon	Dr. Earl M. Pallett, Board of Higher Education, Basic Science Examining Committee, Box 5175, Eugene.
Rhode Island	Mr. Thomas B. Casey, Div. of Professional Regulation, 366 State Office Building, Providence.
South Dakota	Dr. Gregg M. Evans, 310 E. 15th St., Yankton.
Tennessee	Dr. O. W. Hyman, 62 S. Dunlap St., Memphis 5.
Texas	Dr. Cornelia M. Smith, State Office Bldg., 201 E. 14th St., Austin.
Washington	Mr. Thomas A. Carter, Dept. of Licenses, Capitol Building, Olympia.
Wisconsin	Mr. William H. Barber, 621 Ranson St., Ripon.

NATIONAL BOARD OF MEDICAL EXAMINERS

The National Board of Medical Examiners, founded in 1915, includes in its membership representatives from the Federation of State Medical Boards of the United States, the Council on Medical Education and Hospitals of the American Medical Association, the Association of American Medical Colleges, the Armed Services, and the Veterans Administration. Members at large are elected from among leaders in medicine throughout the country. The purpose of this examining agency is to prepare and administer qualifying examinations of such high quality that legal agencies governing the practice of medicine within each state may, in their discretion, grant successful candidates a license without further examination. The National Board is not a licensing body. It is the function of the individual states to determine who shall practice within their borders and to maintain high standards of medical practice, in accordance with their own rules and regulations.

The certificate of the National Board is accepted as an adequate qualification by the medical licensing authorities of the states, the District of Columbia, and outlying possessions, except in: Arkansas, Florida, Georgia, Indiana, Louisiana, Michigan, and North Carolina. Texas and Delaware accept National Board certification if the diplomate has been licensed in some other state. New Jersey requires that the grade in each subject should be at least 75%, even for those who have obtained a passing average on National Board examinations and have been certified as National Board diplomates. New York allows only one grade below 70%. Georgia accepts National Board certificates issued prior to October, 1953. Michigan endorses National Board examinations, with a special written supplemental examination, if parts 1 and 2 were completed prior to Nov. 1, 1954. Supplementary oral examinations are required in Illinois, Rhode Island, and Wyoming. In addition, the laws of 11 of the boards of examiners in the basic sciences are

TABLE 32.—*Graduates of Foreign Medical Faculties Representing Additions to the Medical Profession, 1959*

	Examination	Reciprocity and Endorsement	Total
Alabama	69	0	69
Arizona	5	0	5
California	66	0	66
Canal Zone	0	1	1
Colorado	2	0	2
Connecticut	117	0	117
Delaware	1	0	1
District of Columbia	4	10	14
Florida	11	0	11
Georgia	14	0	14
Hawaii	7	0	7
Illinois	315	0	315
Indiana	15	1	16
Iowa	5	1	6
Kansas	4	0	4
Maine	18	0	18
Maryland	62	0	62
Massachusetts	26	0	26
Michigan	33	0	33
Minnesota	9	0	9
Mississippi	1	0	1
Missouri	25	0	25
Montana	1	0	1
Nebraska	1	0	1
New Hampshire	2	1	3
New Jersey	102	0	102
New Mexico	1	0	1
New York State	255	2	257
North Carolina	1	0	1
North Dakota	3	0	3
Ohio	67	0	67
Pennsylvania	33	0	33
Puerto Rico	114	0	114
Rhode Island	22	0	22
South Dakota	6	0	6
Tennessee	1	0	1
Texas	31	0	31
Virginia	94	0	94
Virgin Islands	1	0	1
Washington	18	4	22
West Virginia	2	0	2
Wisconsin	11	1	12
Totals	1,605	21	1,626

TABLE 33.—*Additions to the Medical Profession Representing Graduates of Foreign Medical Faculties 1950-1959*

Year	Examination	Reciprocity and Endorsement	Totals
1950	267	41	308
1951	425	25	450
1952	545	24	569
1953	662	23	685
1954	749	23	772
1955	881	26	907
1956	834	18	852
1957	991	23	1,014
1958	1,129	37	1,166
1959	1,605	21	1,626
Totals	8,088	261	8,349

sufficiently broad to enable them to accept the examination of the National Board and other state boards in lieu of their own. These include the boards of Alaska, Arkansas, Connecticut, Iowa, Kansas, Minnesota, Nebraska, Oklahoma, Tennessee, Wisconsin, and the District of Columbia. Nebraska reserves the right to review the questions and answers of the applicant; and, if these are satisfactory, they may be accepted.

The National Board admits to its examination students and graduates of approved medical schools in the United States and Canada. The National Board does not admit any graduates of medical schools outside of the United States and Canada to its examinations leading to certification. Upon receipt of a request initiated by a state licensing board, a specialty board, or a medical school, an individual may be admitted to National Board examinations in order to satisfy special requirements or regulations of the licensing board, specialty board, or the medical school. In such cases, the individual is not considered a candidate for certification. He is admitted to the examination as a service to the agency initiating the request, and the grades are sent only to that body.

The examinations are divided into three separate parts: Part 1, Part 2, and Part 3. There is no time limitation between the parts. Part 1 consists of a written examination in each of the following six subjects: Anatomy, including Histology and Embryology; Physiology; Biochemistry; Pathology; Bacteriology, including Immunology; Pharmacology and Materia Medica. A candidate is eligible for Part 1 who has completed the formal courses of the first two years in an approved medical school. Unless required by his medical school to take all six subjects at one examination period, a candidate may, if he so elects, take a divided examination by taking four or five subjects at one time and the remaining one or two at a subsequent time. Part 2 is likewise a written examination in each of the following subjects: Medicine; Psychiatry and Legal Medicine; Surgery; Obstetrics and Gynecology; Public Health and Preventive Medicine; and Pedi-

TABLE 34.—*States Having Basic Science Legislation*

		Subjects Included								Interstate Registration Policies																						
	Year of Enactment	Anatomy	Bacteriology	Chemistry	Diagnosis	Hygiene	Pathology	Physiology	Public Health	Alaska	Arizona	Arkansas	Colorado	Connecticut	District of Columbia	Florida	Iowa	Kansas	Michigan	Minnesota	Nebraska	Nevada	New Mexico	Oklahoma	Oregon	Rhode Island	South Dakota	Tennessee	Texas	Washington	Wisconsin	Other
Alaska	1916	x	x	x	..	x	x	x	..	..	..	x	x	x	x	..	..	x	x	x	..	x	..	x	x	..	..	x	x	x	x	
Arizona	1936	x	x	x	..	x	x	x	..	Reciprocity if credentials equal to those of Arizona and 4 subjects passed at one time																						
Arkansas	1929	x	x	x	..	x	x	x	..	x	x	..	x	..	..	..	..	x	x	x	..	x	x	x	x	..	x	x	x	x	x	
Colorado	1937	x	x	x	..	..	x	x	..	x	x	x	..	x^{1}	x	..	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x^{1}	
Connecticut	1925	x	..	..	x	x	x	x	..	No reciprocity^{2}																						
District of Columbia	1929	x	x	x	..	..	x	x	..	Examination may be waived^{3}																						
Florida	1939	x	x	x	..	..	x	x	..	No reciprocity																						
Iowa	1935	x	x	x	..	x	x	x	..	*Exemption* if credentials equal to those of Iowa^{3}																						
Kansas	1957	x	x	x	..	..	x	x	..	Examination may be waived^{3} ^{4}																						
Michigan	1937	x	x	x	..	..	x	x	..	x	x	x	x	..	x	..	x	x	..	x	x	x	x	..	x	x^{4}	x	x	x	x	x^{1}	
Minnesota	1927	x	x	x	..	x	x	x	..	x^{3}	x^{3}	..	x	x^{3}	x^{5}	..	..	..	x^{3}	..	x	x^{3}	x^{3}	x^{3}	x	..	x^{3}	x	x^{3}	x^{3}	x^{3}	
Nebraska	1927	x	x	x	..	x	x	x	..	May waive examination if basic science or medical grades of other states not less than 75% in each subject																						
Nevada	1951	x	x	x	..	..	x	x	..	..	x	x	x	..	..	x	x	..	x	x	x	..	x	x	x	..	x	x	x	x	x^{1}	
New Mexico	1941	x	x	x	..	..	x	x	..	..	x	x	x	..	..	..	x^{7}	..	x	x	..	x	..	x	x	x^{7}	x	..	..	x^{7}	x^{7}	
Oklahoma	1937	x	x	x	..	..	x	x	..	Considered on individual basis																						
Oregon	1934	x	x	x	..	x	x	x	..	..	x	x	x	..	..	..	x	..	x	x	x	x	x	x	..	..	x	x	x	x	x	
Rhode Island	1940	x	x	x	..	..	x	x	..	..	..	x	x	..	x	..	..	..	..	..	..	..	..	x	..	..	..	..	..	..	..	
South Dakota	1939	x	x	x	..	..	x	x	..	x	x	x	x	..	..	..	x	x	x	x	x	x	x	x	x	x	..	x	x	x	x	
Tennessee	1943	x	x	x	..	..	x	x	..	x	x	..	x	..	x	..	..	..	x	x	x	x	..	x	x	..	x	..	x	x	..	
Texas	1949	x	x	x	..	x	x	x	x	x	x	x	x	..	..	..	x	..	x	x	x	x	..	x	x	..	x	x	..	x	x^{5}	
Washington	1927	x	x	x	..	x	x	x	..	x	x	x	x^{7}	..	x^{7}	..	x^{3}	..	x	x	x^{3}	x^{7}	x^{7}	x^{7}	x^{7}	x^{7}	x^{7}	x^{7}	x	..	x^{7}	
Wisconsin	1925	x	..	..	x	..	x	x	..	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	^{8}

1. Candidates required to pass examinations in Chemistry *and* Bacteriology.
2. Certificate by endorsement obtainable by diplomates of National Board of Medical Examiners or to candidates holding a license obtained by examination in another state after three years *professional* activity.
3. Each case considered individually.
4. *Prior to Jan. 13, 1958.*
5. Must take examination in Bacteriology, Chemistry and Hygiene.
6. Applicants holding state licenses from California, Indiana, Kansas, Kentucky, New York, Vermont and West Virginia considered on individual *basis. Partial reciprocity* to those presenting state licenses from Alabama, Georgia, Louisiana and Maryland. Part I of examination of National Board of Medical Examiners accepted *for* reciprocity.
7. Limited reciprocity.
8. Examination waived if candidate has passed Part I of examination of National Board of Medical Examiners, and to commissioned officers *of the armed forces or the* Public Health Service, candidates from states not having a basic science law presenting state licenses considered on an individual basis; also physicians licensed in Canada.

x Implies yes.

atrics. A candidate is eligible for Part 2 who has completed or has nearly completed a four year medical course in an approved medical school.

TABLE 35.—*Candidates Examined in Basic Sciences, 1959*

	Examined	Passed	Failed	% Failed
Alaska	5	2	3	60.0
Arizona	88	88	*	..
Arkansas	85	74	11	12.9
Colorado	170	170	*	..
Connecticut	226	179	47	20.8
District of Columbia	21	20	1	4.8
Florida	973	658	315	32.4
Iowa	125	31	94	75.2
Kansas	74	54	20	27.0
Michigan	539	361	178	33.0
Minnesota	341	289	52	15.2
Nebraska	171	119	52	30.4
Nevada	125	82	43	34.4
New Mexico	91	57	34	37.4
Oklahoma	148	83	65	43.9
Oregon	167	110	57	34.1
Rhode Island	110	99	11	10.0
South Dakota	185	116	69	37.3
Tennessee	200	172	28	14.0
Texas	294	245	49	16.6
Washington	244	185	59	24.1
Wisconsin	201	121	80	39.8
Totals	4,583	3,315	1,268	27.7

* Failure data not reported.

Part 3 is a clinical and practical evaluation of the candidate's ability in observation, in diagnostic acumen, and in the principles of therapy. The examination provides an opportunity for each candidate to demonstrate his ability to apply his knowledge of clinical problems in the following four major elements of general practice: Clinical Medicine; Pediatrics; Clinical Surgery; and Obstetrics, and Gynecology. A candidate is eligible for Part 3 if he has passed Parts 1 and 2, received the degree of Doctor of Medicine, and served at least one year in a hospital approved for intern training.

TABLE 36.—*Basic Science Certificates Issued by Examination, Reciprocity, Endorsement, Exemption, or Waiver, 1959*

	Certified		
	Examination	Reciprocity, Endorsement, Exemption, or Waiver	Total Certified
Alaska	2	22	24
Arizona	88	191	279
Arkansas	74	40	114
Colorado	170	89	259
Connecticut	179	132	311
District of Columbia	20	167	187
Florida	658	0	658
Iowa	31	178	209
Kansas	54	63	117
Michigan	361	334	695
Minnesota	289	159	448
Nebraska	119	23	142
Nevada	82	34	116
New Mexico	57	34	91
Oklahoma	83	0	83
Oregon	110	77	187
Rhode Island	99	1	100
South Dakota	116	44	160
Tennessee	172	117	289
Texas	245	500	745
Washington	185	235	420
Wisconsin	121	240	361
Totals	3,315	2,680	5,995

TABLE 37.—*Candidates for Basic Science Certification, 1927-1959*

	No. of Boards	Examination			Reciprocity, Endorsement, Exemption, or Waiver	Total Certified
		Passed	Failed	% Failed.		
1927	5	294	33	10.0	27	321
1928	5	617	88	12.4	19	636
1929	7	641	93	12.6	75	716
1930	7	636	127	16.6	122	758
1931	7	634	153	19.4	141	775
1932	7	634	101	13.7	118	752
1933	8	557	104	15.7	131	688
1934	9	751	115	13.3	138	889
1935	10	794	162	16.8	114	908
1936	10	917	181	16.4	243	1,160
1937	12	1,102	242	18.0	202	1,304
1938	12	1,096	230	17.3	293	1,389
1939	14	1,110	249	18.3	1,021	2,131
1940	16	1,293	290	18.3	346	1,639
1941	17	1,751	373	17.5	353	2,104
1942	17	1,725	497	22.3	304	2,029
1943	18	2,309	410	15.1	382	2,691
1944	18	2,144	605	22.0	309	2,453
1945	18	2,339	634	21.3	584	2,923
1946	19	2,558	692	21.2	1,474	4,032
1947	19	2,633	905	25.6	960	3,593
1948	19	3,038	789	20.6	1,418	4,456
1949	20	3,656	1,515	29.5	1,480	5,136
1950	20	3,430	1,340	28.1	2,526	5,956
1951	21	3,198	735	18.7	1,939	5,137
1952	21	3,806	1,346	26.1	1,924	4,730
1953	21	3,854	1,220	24.0	1,899	5,753
1954	21	3,941	874	18.2	1,976	5,917
1955	21	3,474	447	11.1	1,936	5,410
1956	21	3,734	741	16.6	2,373	6,107
1957	22	4,024	842	17.3	2,283	6,307
1958	22	3,592	1,008	21.9	2,677	6,269
1959	22	3,315	1,268	27.7	2,680	5,995
Totals		69,597	18,409	20.9	32,467	101,064

Under special circumstances, consideration may be given to service in a laboratory of a nature acceptable to the National Board as the equivalent of hospital service. Part 3 is administered in 38 centers throughout the United States. Parts 1 and 2 are held at approved medical schools in the United States and Canada.

TABLE 38.—*Basic Science Registration Fees*

Alaska	$25	Nebraska	$10[3]
Arizona	20	Nevada	25
Arkansas	25[1]	New Mexico	50[4]
Colorado	25	Oklahoma	15[2]
Connecticut	25	Oregon	25
District of Columbia	25	Rhode Island	10
Florida	10	South Dakota	15
Iowa	10	Tennessee	25[5]
Kansas	25	Texas	25[6]
Michigan	10	Washington	10
Minnesota	25[2]	Wisconsin	10[3]

Fee for registration without examination and for nonresidents: [1] nonresidents $50; [2] reciprocity $50; [3] waiver $15; [4] reciprocity $75; [5] reciprocity $10; [6] reciprocity and waiver $50.

Examinations in Part 1 were held, during 1959, in June and September and, in Part 2, in April and June. Beginning in 1960, the Part 2 examination is to be held in April only. Part 3 is held during the latter part of June of each year. An interim examination is usually scheduled in Part 3 during the autumn or winter.

In the following paragraphs, data are presented regarding the examinations conducted and the issuance of certificates by the National Board. This is the 38th annual compilation of these statistics. The board's first examination was given in October, 1916. From that date and up to and including a test given in June, 1921, 11 examinations were given, and 268 candidates were certified. Since 1922, the examination has been given in three parts.

The results of examinations given in Parts 1 and 2 during 1959 and the results for each year since 1922 are recorded in tables 39 and 40. The data shown in these tables represent examinations conducted rather than persons examined. The figures, thus, include candidates who fail and are reexamined during the same year and those who may pass Parts 1 and 2 in the same year.

TABLE 39.—*National Board Examinations in Part 1, 1922-1959*

Date	Total Examinations	Passed	Incomplete	Failed	% Failed
June, 1959	3,259	2,102	873	284	11.9
September, 1959	1,112	394	670	48	10.9
Totals	4,371	2,496	1,543	332	11.7
1922	388	263	58	67	20.3
1923	507	319	77	81	18.8
1924	591	415	69	107	20.5
1925	608	400	50	158	28.3
1926	625	436	104	85	16.3
1927	702	452	159	91	16.8
1928	843	533	231	79	12.9
1929	1,096	675	331	90	11.8
1930	1,260	801	345	114	12.5
1931	1,277	755	425	97	11.4
1932	1,307	847	371	89	9.5
1933	1,234	782	316	136	14.8
1934	1,241	809	347	85	9.5
1935	1,264	785	410	69	8.1
1936	1,314	858	363	123	12.5
1937	1,435	871	415	149	14.6
1938	1,654	986	508	160	14.0
1939	1,733	1,048	460	225	17.7
1940	1,653	1,069	375	209	16.4
1941	1,640	1,087	346	207	16.0
1942	1,867	1,204	471	192	13.8
1943	2,656	1,441	962	253	14.9
1944	4,229	2,326	1,465	438	15.9
1945	3,865	2,106	1,475	284	11.8
1946	3,148	1,695	1,189	264	13.5
1947	3,514	1,844	1,352	318	14.7
1948	3,807	2,178	1,262	367	14.4
1949	3,823	2,337	1,243	243	9.4
1950	3,678	2,358	986	334	9.0
1951	3,520	2,153	1,038	329	9.3
1952	3,989	2,467	1,147	375	9.4
1953	4,278	2,866	980	432	13.0
1954	3,252	2,286	677	289	11.2
1955	3,196	1,735	1,173	288	14.2
1956	3,475	2,675	510	290	10.8
1957	3,816	2,281	1,311	224	8.9
1958	4,210	2,443	1,430	337	12.1
1959	4,371	2,496	1,543	332	11.7
Totals	87,096	53,112	25,974	8,010	13.1

In 1959, 4,371 examinations were given in Part 1; 2,496 passed, and 332 (11.7%) failed. There were 1,543 incomplete examinations given. In Part 2, 2,881 examinations were held; 2,767 passed, and 73 (2.6%) failed. Incomplete examinations are seldom given in Part 2. There were 41 such examinations given in 1959.

TABLE 40.—*National Board Examinations in Part 2, 1922-1959*

Date	Total Examinations	Passed	Incomplete	Failed	% Failed
April, 1959	2,526	2,442	23	61	2.4
June, 1959	355	325	18	12	3.6
Totals	2,881	2,767	41	73	2.6
1922	109	90	0	19	17.4
1923	192	170	2	20	10.5
1924	267	227	0	40	15.0
1925	342	309	0	33	9.6
1926	381	334	1	46	12.1
1927	361	314	1	46	12.8
1928	410	371	1	38	9.3
1929	465	399	19	47	10.5
1930	620	543	7	70	11.4
1931	719	630	2	87	12.1
1932	732	674	0	58	7.9
1933	714	651	0	63	8.8
1934	633	583	0	50	7.9
1935	689	620	0	69	10.0
1936	768	716	2	50	6.5
1937	855	803	1	51	6.0
1938	861	815	0	46	5.3
1939	938	884	0	54	5.8
1940	1,028	963	9	56	5.5
1941	1,001	954	1	46	4.6
1942	1,072	1,031	0	41	3.8
1943	1,861	1,805	0	56	3.0
1944	1,405	1,350	0	55	3.9
1945	1,599	1,565	0	34	2.1
1946	1,825	1,782	0	43	2.4
1947	1,641	1,613	0	28	1.7
1948	1,742	1,725	0	17	0.9
1949	1,737	1,691	0	46	2.6
1950	1,863	1,837	0	26	1.3
1951	2,045	2,017	0	28	1.4
1952	2,017	2,001	0	16	0.8
1953	2,200	2,145	1	54	2.4
1954	2,258	2,169	26	63	2.8
1955	2,220	2,181	3	36	1.6
1956	2,182	2,153	3	26	1.2
1957	2,151	2,115	18	18	0.8
1958	2,625	2,540	15	64	2.5
1959	2,881	2,767	41	73	2.6
Totals	47,403	45,537	153	1,713	3.6

Since 1922, a total of 87,906 examinations have been given in Part 1 and 47,403 in Part 2. During this period, 53,112 passed Part 1, and 45,537 passed Part 2. In the 38-year period shown, there have been 8,010 failures in Part 1 (13.1%) and 1,713 failures in Part 2 (3.6%).

In 1959, 2,326 tests were given in Part 3; 2,317 passed, and 9 (0.4%) failed. Results of examinations in Part 3, in 1959 and in the 37 preceding years, are given in table 41. In 38 years, 41,012 were tested; 40,153 were granted the certificate of the board. The percentage of failures in this final examination in 38 years was 2.1. The 2,317 physicians certified as diplomates in 1959 represented 68 medical schools in the United States and 8 medical schools in Canada. The schools and the number of examinees from each are included in table 42.

In 1959, there were 3,377 licenses to practice medicine issued by endorsement of the certificate of the National Board of Medical Examiners by 43 state boards, the District of Columbia, Canal Zone, and Puerto Rico. The number registered by each of these licensing boards is recorded in table 43. There have been 45,047 licenses issued on the basis of endorsement of the board's certificate by the various states, territories, and outlying possessions since 1915.

In addition to its traditional function of administering examinations to individual candidates for the National Board's certificate, the National Board is being called upon more and more to provide examinations for medical schools for a variety of purposes. The most prevalent use of the examination in medical schools is for the purpose of a valid, comprehensive, and impartial evaluation of the student class at the end of the second year (Part 1) or at the end of the fourth year (Part 2). In some schools, an individual department may add a National Board test to its own departmental appraisal of its students in a particular subject. There were 43 medical schools in which Part 1, Part 2, or both parts of the National Board examinations were taken by at least 75% of the students in the classes involved during 1959.

TABLE 41.—*National Board Examinations in Part 3, 1922-1959*

Year	Total Examinations	Passed	Failed	% Failed
1922	22	22	0	0.0
1923	82	81	1	1.2
1924	126	120	6	4.8
1925	219	206	13	5.9
1926	255	243	12	4.7
1927	293	272	21	7.2
1928	322	306	16	5.0
1929	352	337	15	4.3
1930	420	401	19	4.5
1931	437	419	18	4.1
1932	550	522	28	5.1
1933	551	526	25	4.5
1934	567	548	19	3.4
1935	598	578	20	3.3
1936	576	547	29	5.0
1937	668	630	38	5.7
1938	706	682	24	3.4
1939	770	729	41	5.3
1940	792	771	21	2.7
1941	910	885	25	2.7
1942	1,054	1,041	13	1.2
1943	1,230	1,213	17	1.4
1944	1,168	1,146	22	1.8
1945	1,245	1,232	13	1.0
1946	1,634	1,613	21	1.2
1947	1,741	1,723	18	1.0
1948	1,715	1,700	15	0.9
1949	1,685	1,674	11	0.6
1950	1,752	1,736	16	0.9
1951	1,738	1,708	30	1.7
1952	2,128	2,036	92	4.3
1953	3,039	1,979	60	2.9
1954	2,133	2,052	81	3.8
1955	2,090	2,077	13	0.6
1956	2,085	2,072	13	0.6
1957	2,010	1,998	12	0.6
1958	2,023	2,011	12	0.6
1959	2,326	2,317	9	0.4
Totals	41,012	40,153	859	2.1

TABLE 42.—*Diplomates from Individual Medical Schools, 1959*

United States	
Medical College of Alabama	6
University of Arkansas	4
College of Medical Evangelists	47
University of California, Los Angeles	1
University of Southern California	16
Stanford University	18
University of California, San Francisco	3
University of Colorado	3
Yale University	71
Georgetown University	83
George Washington University	89
Howard University	20
University of Miami	26
Chicago Medical School	69
Northwestern University	54
Stritch School of Medicine	29
University of Chicago	45
University of Illinois	83
Indiana University	1
State University of Iowa	4
University of Kansas	35
University of Louisville	16
Johns Hopkins University	18
University of Maryland	5
Boston University	61
Harvard Medical School	141
Tufts University Medical School	111
University of Michigan	7
University of Minnesota	1
University of Missouri	2
St. Louis University	25
Washington University	4
Creighton University	24
University of Nebraska	2
Albany Medical College	63
University of Buffalo	79
Columbia University	111
Cornell University	77
New York Medical College	114
New York University	129
State University of New York, Brooklyn	150
University of Rochester	71
State University of New York, Syracuse	67
Duke University	10
Bowman-Gray School of Medicine	1
University of Cincinnati	2
Western Reserve University	27
Ohio State University	1
University of Oregon	16
Hahnemann Medical College	8
Jefferson Medical College	13
Temple University	7
University of Pennsylvania	45
Woman's Medical College	18
University of Pittsburgh	1
University of Puerto Rico	21
Medical College of South Carolina	1
University of Tennessee	3
Meharry Medical College	3
Southwestern Medical School	2
Baylor University	1
University of Utah	4
University of Vermont	39
University of Virginia	1
Medical College of Virginia	1
University of Washington	10
University of Wisconsin	5
Marquette University	7
Total	2,242
Canada	
University of British Columbia	6
University of Manitoba	4
Dalhousie University	5
Queen's University	1
University of Western Ontario	2
University of Ottawa	3
University of Toronto	9
McGill University	45
Total	75

The officers of the board are Walter A. Bloedorn, M.D., President; Samuel M. Poindexter, M.D., Vice President; John P. Hubbard, M.D., Executive Secretary and Treasurer; William V. Clemans, Ph.D., Director of Testing Services; Christian J. Lambertsen, M.D., Assistant Secretary for Part 1; George D. Ludwig, M.D., Board Relations. The address of the board is 133 S. 36th St., Philadelphia 4.

TABLE 43.—*Licenses Granted on the Basis of National Board Certificates, 1959*

Alabama	12
Alaska	9
Arizona	20
California	659
Colorado	26
Connecticut	189
Delaware	2
District of Columbia	78
Georgia	4
Hawaii	26
Idaho	10
Illinois	128
Iowa	7
Kansas	14
Kentucky	21
Maine	25
Maryland	65
Massachusetts	307
Michigan	20
Minnesota	67
Mississippi	5
Missouri	30
Montana	10
Nebraska	1
Nevada	4
New Hampshire	23
New Jersey	180
New Mexico	5
New York	952
North Dakota	3
Ohio	84
Oklahoma	5
Oregon	24
Pennsylvania	120
Rhode Island	27
South Carolina	9
Tennessee	9
Utah	19
Vermont	9
Virginia	58
Washington	40
West Virginia	15
Wisconsin	23
Wyoming	2
Canal Zone and Puerto Rico	21
Totals	3,377

EDUCATIONAL COUNCIL FOR FOREIGN MEDICAL GRADUATES

The Educational Council for Foreign Medical Graduates gave two of its American Medical Qualification Examinations in 1958 and two in 1959. The results of these examinations are given in table 44.

In the first examination (March 25, 1958), 68% of the 298 candidates attained scores of 70% or above; 51% attained scores of 75% or above. In the second examination (Sept. 23, 1958), 76.3% of the 844 candidates attained scores of 70% or above; 49.5% attained scores of 75% or above. In the third examination (Feb. 17, 1959), 68.8% of the 1,772 candidates attained scores of 70% or above; 43.4% attained scores of 75% or above. In the fourth examination (Sept. 22, 1959), 68.8% of the 3,068 candidates attained scores of 70% or above; 44.7% attained scores of 75% or above.

As of Jan. 1, 1960, the Educational Council for Foreign Medical Graduates had examined 5,982 foreign medical graduates. Of these, 2,709 had been granted the standard certificate; 1,419 had been granted temporary (two-year) certificates.

Examination centers have been established in 66 cities outside continental United States and 35 cities in the United States. Of the foreign examination centers, 19 were in Europe, 17 in Latin America, 11 in the Far East, 10 in the Near and Middle East, 6 in Africa, and 2 in Oceania. A list of the examination centers in which the examination may be taken is included in table 45.

The present policy of the Council on Medical Education and Hospitals regarding Educational Council for Foreign Medical Graduates certification for foreign medical graduates serving as interns or residents is based upon a fundamental concern for the welfare of patients. This policy was published in The Journal[5] and mailed to hospitals and other agencies interested in the foreign medical graduate. A statement applicable to foreign medical graduates serving in a capacity other than interns or residents appeared in The Journal[6] shortly after the policy statement.

Table 44.—*American Medical Qualifying Examination of Educational Council for Foreign Medical Graduates*

Examination		Granted Standard Certificate		Granted Temporary Certificate		Total 70 or Above	
	No.	No.	%	No.	%	No.	%
March 25, 1958	298	152	51	0	0	203	68
September 23, 1958							
United States	707	371	52.4	193	27.3	564	79.8
Abroad	137	47	34.3	33	24.1	80	58.4
Total	844	418	49.5	226	26.8	644	76.3
February 17, 1959							
United States	1,278	616	48.2	341	26.7	957	74.9
Abroad	494	153	31.0	110	22.3	263	53.2
Total	1,772	769	43.4	451	25.5	1,220	68.8
September 22, 1959							
United States	2,351	1,088	46.3	601	25.6	1,689	71.8
Abroad	717	282	39.3	141	19.7	423	59.0
Total	3,068	1,370	44.7	742	24.2	2,112	68.8

Table 45.—*List of Examination Centers for American Medical Qualifying Examination*

United States Centers
California, Los Angeles
San Francisco
Colorado, Denver
Connecticut, New Haven
D. C., Washington
Florida, Gainesville
Miami
Georgia, Emory
Hawaii, Honolulu
Illinois, Chicago
Kansas, Kansas City
Kentucky, Louisville
Maryland, Baltimore
Massachusetts, Boston
Michigan, Ann Arbor
Minnesota, Minneapolis
Missouri, St. Louis
Nebraska, Omaha
New Jersey, Jersey City
New York, Brooklyn
Buffalo
New York City
Syracuse
North Carolina, Durham
North Dakota, Grand Forks
Ohio, Cincinnati
Cleveland
Oklahoma, Oklahoma City
Pennsylvania, Philadelphia
Pittsburgh
Tennessee, Nashville
Texas, Houston
Virginia, Richmond
Washington, Seattle
Wisconsin, Milwaukee
Puerto Rico, San Juan
Canada, Montreal
Foreign Centers
Latin America
Argentina, Buenos Aires
Netherland Antilles, Aruba
Brazil, Rio de Janeiro
Chile, Santiago
Colombia, Cali
Costa Rica, San Jose
Ecuador, Quito
Haiti, Port-au-Prince
Mexico, D. F. (Mexico City)
Bahama Islands, Nassau
Nicaragua, Managua
Panama, Panama City
Paraguay, Asuncion
Peru, Lima
El Salvador, San Salvador
Venezuela, Caracas
Far East
Hong Kong
India, Bombay
Calcutta
Madras
New Delhi
Japan, Tokyo
Korea, Seoul
Philippines, Manila
Asia, Singapore
Taiwan, Taipei
Thailand, Bangkok
Near and Middle East
Cyprus, Nicosia
Iran, Tehran
Israel, Tel Aviv
Lebanon, Beirut
Pakistan, Dacca
Karachi
Lahore
Syria, Damascus
Turkey, Ankara
Istanbul
Oceania
Australia, Canberra
New Zealand, Wellington
Europe
Austria, Vienna
Belgium, Brussels
Denmark, Copenhagen
England, London
France, Paris
Germany, Berlin
Bonn
Frankfurt
Munich
Greece, Athens
Iceland, Reykjavik
Ireland, Dublin
Italy, Rome
Netherlands, The Hague
Portugal, Lisbon
Scotland, Edinburgh
Spain, Madrid
Switzerland, Bern
Yugoslavia, Belgrade
Africa
Egypt, Cairo
French West Africa, Dakar
Ghana, Accra
Kenya, Nairobi
South Africa, Johannesburg
Belgian Congo, Leopoldville

The Executive Director of the Educational Council for Foreign Medical Graduates is Dr. Dean F. Smiley, 1710 Orrington Ave., Evanston, Ill.

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3. Medical Education in United States and Canada, Council on Medical Education and Hospitals, J. A. M. A. **171:** 1514-1517 (Nov. 14) 1959.

4. An Open-Ended Medical Education, Editorial, J. A. M. A. **171:**1576-1577 (Nov. 14) 1959.

5. Council on Medical Education and Hospitals Policy for Foreign Medical Graduates, J. A. M. A. **172:**1045 (March 5) 1960.

6. Foreign Medical Graduates Other Than Interns and Residents, Report of Council on Medical Education and Hospitals, J. A. M. A. **172:**1397 (March 26) 1960.

MEDICAL NEWS

CALIFORNIA

New Medical Center.—The establishment of a new medical center took place May 1, when the existing Stanford Hospital in San Francisco became the Presbyterian Medical Center. The center announced that there will be no disruption in the handling of accounts, as the new corporation will pay any outstanding obligations under the arrangement between the two organizations. For information, write the Presbyterian Medical Center, San Francisco 15.

State Law Against Pollution by Autos.—The Los Angeles County Air Pollution Control District announced that with the passage of Assembly Bill No. 17 on April 5 California became the first state to take legislative action against pollution of the atmosphere by the automobile. The bill requires devices on all new cars throughout the entire state, but allows counties not affected by smog to exclude themselves from the provisions concerning used cars. In order to exclude a county, its board of supervisors must establish at a public hearing that there is no air pollution problem in that county. Every two years thereafter, a hearing must be held again to reaffirm the absence of an air pollution problem. The metropolitan counties, which are most likely to come under the law, have vehicle registrations of about 6.6 million, while the total registration in the nonmetropolitan counties is only about 1.4 million. The law sets up a timetable for installation of devices. Measured from the day a state board certifies that at least two devices are approved, this is the schedule:

1. Within one year—a. All new vehicles throughout the state, when first registered. b. Used vehicles, located in a county affected by the law, if there is a transfer of ownership.
2. Within two years—All used commercial vehicles, located in a county affected by the law.
3. Within three years—All motor vehicles, located in a county affected by the law.

Automobiles are estimated to contribute daily about 1,500 tons of hydrocarbons (exclusive of evaporation loss), about 450 tons of oxides of nitrogen, and about 9,000 tons of carbon monoxide.

DISTRICT OF COLUMBIA

Awards for "Statesmanship in Health."—An awards luncheon will be held Wednesday, June 1, at the Statler–Hilton Hotel, Washington, arranged by the following honorary chairmen and members of the executive committee for "Health-USA" Awards: Dr. Victor R. Alfaro, president, Medical Society of the District of Columbia; E. K. Morris, president, Washington Board of Trade; Ralph E. Becker, director, Washington Board of Trade; Dr. W. LeRoy Dunn, past-president, Medical Society of the District of Columbia; Dr. Oscar B. Hunter Jr., director, Hunter Memorial Laboratory; and Dr. Richard T. Sullivan, chairman, Public Health Committee, Washington Board of Trade. The "Health-USA" Awards annually honor "Statesmanship in Health." Three awards will be made at the luncheon: Major Gen. Howard M. Snyder, physician to President Eisenhower, for his contributions to medicine in serving the President; Elmer Bobst, chairman of the board, Warner–Lambert Pharmaceutical Company, for his efforts in drug research and leadership in the development of the American Cancer Society; Dr. Donald H. Stubbs, chairman of the board (national), Blue Shield Voluntary Insurance Plan, for his activities and interest in the health insurance field and particularly in the advancement of the Federal Government Health Insurance Plan for Government Employees. "Health-USA" Awards are sponsored by the Washington Board of Trade and the Medical Society of the District of Columbia. For information, write Mr. Henry P. Loss, 1616 K St., N. W., Washington 6, D. C. (STerling 3-3535).

IDAHO

Annual Meeting in Sun Valley.—The 68th annual meeting of the Idaho State Medical Association will be held June 15-18 at Sun Valley, under the presidency of Dr. Quentin W. Mack, Boise. Program director is Dr. A. Curtis Jones, who announced the following guest speakers for the program: Drs. Lewis L. Robbins, Glen Oaks, N. Y.; D. L. C. Bingham, Kingston, Ont., Canada; M. Digby Leigh, Los Angeles; James W. Warren, Galveston, Texas; and Milton L. McCall, Pittsburgh. A program of entertainment includes golf, tennis, fishing, skeet shooting, and other activities. For information, write Mr. Armand L. Bird, 364 Sonna Bldg., Boise, Idaho, Executive Secretary.

IOWA

Project Provides Medical Information for Students.—The Scott County Medical Society in planning their programs for 1959-1960 decided to set aside one evening for encouragement and recruitment of high school and college students to the field of medicine. In February and March they showed the movie, "I Am A Doctor," to about 3,000 high school

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Physicians are invited to send to this department items of news of general interest, for example, those relating to society activities, new hospitals, education, and public health. Programs should be received at least three weeks before the date of meeting.

and college students in the area, and on May 3 about 60 of the "outstanding" students (with their supervisors) were invited to hear Dr. Robert C. Hardin, professor of internal medicine and acting dean, State University of Iowa College of Medicine, talk on "Careers in Medicine" and Dr. W. W. Morris, associate dean in charge of student affairs, talk on the problem of admissions and admission requirements. Following this the doctors and students asked questions of the speakers for about one hour. Dr. M. J. Brown, of Davenport, was the chairman of the program committee.

MASSACHUSETTS

Dr. Wilkins Named Department Chairman.—Dr. Robert W. Wilkins, of Newburyport, professor of medicine at Boston University's School of Medicine and former president of the American Heart Association, was appointed chairman of the school's department of medicine and physician-in-chief and director of Evans Memorial Department of Clinical Research at the Massachusetts Memorial Hospitals. Dr. Wilkins has served as acting chairman of the department of medicine since Sept. 1 and as associate physician-in-chief, Massachusetts Memorial Hospitals, since 1955. He received the Oscar B. Hunter Memorial Award of the American Therapeutic Society in 1947 "for outstanding work in the field of experimental therapeutics."

NORTH CAROLINA

Dr. Hart Named University President Pro Tem.—Dr. Daryl Hart, chairman, Duke Medical Center's surgery department for 30 years, was named president pro-tem on April 21. He will hold this office with full authority from July 1 until a permanent president is chosen to succeed Hollis Edens, Ph.D., who announced his resignation. Dr. Hart received his M.D. from the John Hopkins Medical School, Baltimore, in 1921. He held various positions at that institution for the next nine years. In 1928 Dr. Hart was offered the surgery department chairmanship in the Duke University School of Medicine, then a new institution still being built in the pine forest west of Durham. He served as president of the Southern Surgical Association in 1956 and as president of the Southern Society of Clinical Surgeons in 1957. He is currently a member of the board of governors, American College of Surgeons.

OHIO

Monthly Seminars to Precede Gerontology Institute.—Ernest W. Retzlaff, Ph.D., assistant professor of physiology and psychiatry, Columbus Psychiatric Institute and Hospital, Ohio State University School of Medicine, announced the first of a series of monthly seminars. This group, sponsored by the Columbus Psychiatric Institute and the department of physiology, has been organized as the first step in establishing a Gerontological Institute which will be primarily concerned with study of the biological aspects of aging.

Dr. Sabin Honored.—Walter C. Langsam, Ph.D., University of Cincinnati president, announced the appointment of Dr. Albert B. Sabin as the university's first distinguished service professor, a new designation created by the UC board of directors to honor Dr. Sabin for his work. Dr. Langsam presented Dr. Sabin with a citation which read: "Eminent authority in research pediatrics, known with gratitude throughout the world as a benefactor of mankind for his achievements in alleviating the scourges of such virus diseases as poliomyelitis, Japanese B-encephalitis, and dengue fever." Dr. Sabin was principal guest of honor and speaker at the citation banquet. His topic was "The Biologist's Dreams—the Humanitarian's Nightmares." He is professor of research pediatrics in UC College of Medicine and fellow of Children's Hospital Research Foundation.

Personal.—Dr. Irvine H. Page, director of research at the Cleveland Clinic and a past-president of the American Heart Association, was appointed to a three-year term on the Expert Advisory Panel on Cardiovascular Diseases of the World Health Organization. Dr. Page is one of four doctors from this country selected to serve on the 39-member panel.——The 103rd Cutter Lecture on Preventive Medicine of the Harvard School of Public Health was given by Dr. Benjamin Pasamanick, professor of psychiatry, Ohio State University College of Medicine. Dr. Pasamanick presented "Epidemiologic Approaches to the Investigation of Childhood Neuropsychiatric Disorder." The Cutter Lectures, presented annually by the Harvard School of Public Health, were established in 1909 through a bequest from Dr. John Clarence Cutter, a graduate of the Harvard Medical School. The lectures have been presented since 1922.

OREGON

Dr. Crane to Succeed Dr. Hunter.—Dr. Warren C. Hunter, a faculty member at the University of Oregon Medical School for 36 years, will retire as professor and chairman of the department of pathology July 1. Dr. Jackson T. Crane, formerly associate professor of pathology and surgery at the University of California School of Medicine, was appointed to take his place. Dr. Hunter will go to the Portland Sanitarium and Hospital on a full-time basis after his retirement, but he will continue to teach at the Medical School on a volunteer basis as a clinical professor of pathology. Dr. Crane received a doctor of medicine degree in 1945 from the University of California. He currently is conducting research on metabolic bone diseases, investigating human and animal dwarfism and other abnormalities of cartilage growth and metabolism.

Cancer Conference in Portland.—The second annual Oregon Cancer Conference will be held July 7 and 8 in Portland under joint sponsorship of the Oregon State Medical Society, Oregon Division of the American Cancer Society, and University of Oregon Medical School. Guest lecturers include Oscar Creech Jr., New Orleans; J. Hartwell Harrison, Boston; Henry L. Jaffe, Los Angeles; I. S. Ravdin, Philadelphia; and R. Wayne Rundles, Durham, N. C. In addition to their individual presentations, each guest speaker will participate in one or more panel discussions. All sessions of the conference will be held in the new Sheraton Hotel in Portland. The entire expense of the conference is being underwritten by the Oregon Division of the American Cancer Society. There will be a charge for the luncheons and banquet. For information, write Mr. Roscoe K. Miller, Executive Secretary, Oregon State Medical Society, 2164 S. W. Park Place, Portland 5.

Primate Research Center.—Two grants totaling $1,917,275 for construction and operation of a regional subhuman primate research center near Portland were made in April to the Medical Research Foundation of Oregon, Inc., by the U. S. Public Health Service. The University of Oregon Medical School will provide the academic environment within which the center will operate. The proposed site is a 163-acre tract about 10 miles west of downtown Portland. The center, to be composed of laboratories and 400 rhesus monkeys, is expected to be in operation by early 1961. The grants were made by the National Heart Institute from funds appropriated by Congress to the National Institutes of Health for the establishment of primate research centers. The center will provide opportunity for basic research in primate genealogy and in related physical and behavioral sciences. It will be a pilot project in what is planned to be a series of such centers. The regional center will be utilized by visiting scientists from many parts of the world. Dr. Donald E. Pickering, Doernbecher Memorial Professor of Pediatrics at the University of Oregon Medical School, and Edward S. West, Ph.D., department of biochemistry, are the principal investigators on the grant.

Personal.—Dr. Edwin E. Osgood, professor of medicine and head of the division of experimental medicine, University of Oregon Medical School, Portland, was named to the clinical fellowship committee of the American Cancer Society.——Dr. Anis M. Behnam, research associate in the division of urology, University of Oregon Medical School, Portland, was selected as a $200 third prize winner in a national essay competition sponsored by the American Urological Association, Inc. He will be honored at the group's annual meeting in May at Chicago.——Dr. Herbert E. Griswold Jr., head, division of cardiology, University of Oregon Medical School, Portland, was appointed to the board of directors of the American Heart Association. He also is on the association's committee on personnel and training.——Dr. Marilyn A. Nelson, 1959 graduate of the University of Oregon Medical School, Portland, was one of 12 women medical students in the United States who graduated first in her class. Now interning at Philadelphia General Hospital, Miss Nelson was awarded $100 by the American Medical Women's Association "in recognition of her distinction." She plans to take a pediatric residency and then practice in Eugene, her home town.——Dr. David K. Taylor, clinical associate in medicine, University of Oregon Medical School, was named secretary of the newly organized Northwest Rheumatism Association, which had its first meeting in November at Portland.

GENERAL

Plastic Surgeons Organize in New England.—The New England Society of Plastic and Reconstructive Surgery was organized and held its first meeting on April 8, in Boston. The following slate of officers was elected: president, Dr. Varaztad H. Kazanjian, Boston; vice-president, Dr. Radford C. Tanzer, Hanover, N. H.; and secretary-treasurer, Dr. Richard P. Sexton, 289 Angell St., Providence, R. I.

Meeting on Research in Ophthalmology.—On June 13-16, the 29th annual meeting of the Association for Research in Ophthalmology, Inc., will be held in Miami, Fla., with headquarters at the Eden Roc Hotel. A total of 28 papers are scheduled on the program, including the Friedenwald Memorial Lecture by Dr. Irving H. Leopold, Philadelphia. Discussions will follow the presentations. The Proctor Medal will be presented to Sir Stewart Duke-Elder, London, England, the morning of June 15, and that evening the awards banquet will be held. For information, write Dr. Lorand V. Johnson, 10515 Carnegie Ave., Cleveland 6, Secretary-Treasurer.

Appoint Nursing Consultant for Heart Group.—Miss Katharine Lembright, R.N., was appointed nursing consultant for the American Heart Association. Miss Lembright, formerly assistant executive secretary of the American Nurses' Association, will plan and develop national programs for improved nursing, especially as they relate to the care of cardiovascular patients. A part-time lecturer on industrial medicine at New York University Postgraduate Medical School, Miss Lembright serves on the American Medical Association's Subcommittee on Industrial Nursing and on the Nursing Committee of the National Society for the Prevention of Blindness.

Geriatric Meeting in Miami Beach.—The 17th annual meeting of the American Geriatrics Society will be held June 9-10 at the Americana Hotel, Miami Beach, Fla., under the presidency of Dr.

Frank Glenn, New York City. Over 20 papers are scheduled on such topics as neurohumoral factors in lipid mobilization, tranquilizers, psychological studies in geriatric hemiplegia, prevention of chronic illness, and nutritional problems in the aged. The annual reception and dinner will be held June 9, 6:30 p. m., at which the Willard O. Thompson Memorial Award will be presented. For information, write Dr. Richard J. Kraemer, 2907 Post Road, Greenwood, Warwick, R. I., Secretary-Treasurer.

Medical Writers' Institute.—The third annual Medical Writers' Institute, for medical writers engaged in serving the medical, pharmaceutical, dental, nursing, and veterinary professions, will be held at the Rensselaer Polytechnic Institute, Troy, N. Y., Monday, June 13 through Friday, June 17. Tuition for the five-day institute will be $175. This fee will cover the instructional part of the program, together with the daily luncheons and the institute dinner. Checks should be made payable to Rensselaer Polytechnic Institute and sent to the Comptroller. Housing will be in the new Freshman Dormitories. Breakfasts may be obtained at the nearby Dining Hall. The enrollment form should be sent as soon as possible to Mr. Jay R. Gould, Director, Medical Writers' Institute, Rensselaer Polytechnic Institute, Troy, N. Y.

Society News.—Dr. C. Paul Hodgkinson, of Detroit, was installed as president of the **American College of Obstetricians and Gynecologists**, succeeding Dr. John I. Brewer, of Chicago. Other officers are first vice-president, Dr. George E. Judd, Los Angeles; second vice-president, Dr. Howard C. Taylor Jr., New York City; treasurer, Dr. Axel N. Arneson, St. Louis; secretary, Dr. Craig W. Muckle, Philadelphia; and assistant secretary, Dr. Sprague H. Gardiner, Indianapolis.——The **American Laryngological Association** installed the following officers for 1960-1961: president, Dr. Edwin N. Broyles, Baltimore; secretary, Dr. Lyman G. Richards, Cambridge, Mass.; treasurer, Dr. Francis E. LeJeune, New Orleans; editor, historian, and librarian, Dr. Francis W. Davison, Danville, Pa. The association's next annual meeting will be held at the Lake Placid Club, Essex County, N. Y., May 21-22, 1961.

Indianapolis and San Bernardino Win Health Awards.—The Indianapolis and the San Bernardino (Calif.) county health departments were judged winners of two top national awards for sanitation programs. The competition was open to more than 1,200 local health departments throughout the country. The Division of Public Health of Marion County, Indiana, which includes the city of Indianapolis, won the Samuel J. Crumbine award for "outstanding achievement" in the development of a program of eating and drinking sanitation. The Crumbine award for the development of a comprehensive program of environmental sanitation was won by the County Health Department of San Bernardino. The annual competition is sponsored by the Public Health Committee of the Paper Cup and Container Institute. The awards are made in memory of Dr. Samuel J. Crumbine, state health officer in Kansas, who was an executive of the American Child Health Association, and one-time executive officer of the Kansas State Board of Health.

Tuberculosis Group Warns Against Cigarettes.—A warning to "all people" of the risk of the development of lung cancer from smoking cigarettes was issued May 4 by the National Tuberculosis Association. The association, which includes all respiratory diseases in its program, pointed out that smoking "appears to be a factor also in such crippling lung diseases as chronic bronchitis and emphysema." Approved by the governing body of the NTA's medical section, the American Trudeau Society, the statement based its worning on three points: "there is an alarming increase in deaths from lung cancer," "cigarette smoking is a major cause of lung cancer," and "the risk of lung cancer increases with the number of cigarettes smoked." It pointed out also that the risk of lung cancer is reduced when smoking is given up. "No present method of treating tobacco or of filtering the smoke has been proved to reduce the harmful effect of cigarette smoking," the statement said. "Up to now, these harmful effects can be avoided only by not smoking cigarettes."

Society News.—The following officers of the **American Society of Facial Plastic Surgery** were elected for the ensuing year: president, Dr. Sam H. Sanders, Memphis, Tenn.; vice-president, Dr. John T. Dickinson, Pittsburgh; secretary, Dr. Samuel M. Bloom, New York City; treasurer, Dr. Joseph C. Miceli, Brooklyn; and chairman of the western section, Dr. W. Eugene Compere Jr., Los Angeles. The annual spring meeting in 1961 will be held from Feb. 11-14 at the Roosevelt Hotel, New Orleans.——The new officers of the **American Radium Society** elected at the recent meeting in San Juan are as follows: president, Dr. Jesshill Love, Louisville, Ky.; president-elect, Dr. Robert L. Brown, Atlanta, Ga.; secretary, Dr. Charles G. Stetson, Englewood, N. J.; and treasurer, Dr. Gilbert H. Fletcher, Houston, Texas.——The officers of the **American Otorhinologic Society for Plastic Surgery, Inc.,** include the following: president, Dr. Thomas E. Briant, Welland, Ont., Canada; secretary, Dr. Joseph G. Gilbert, 75 Barberry Lane, Roslyn Heights, N. Y. The society will meet at the Conrad Hilton Hotel, Chicago, Oct. 9. The 1961 meeting will be held in New York City, March, 1961. European seminars are planned as follows: Paris, July 23-28, 1961; Rome, Aug. 1-3, 1961; Vienna, Aug. 9-11, 1961; Geneva, Aug. 13, 1961; and London, Aug. 17-20, 1961.

Quadrennial Prize for Cancer Research.—The Dr. Raoul Biltris Prize for experimental research on cancer was announced by the Royal Flemish Academy of Medicine of Belgium. The quadrennial prize is for a doctor of medicine with at least 10 years practice, author of an original memoir in manuscript in Dutch, French, English, or German concerning experimental research on cancer. The prize (10,000 fr.) is for the period 1961-1964, ending Dec. 31, 1964. The prize may be awarded every four years. Cooperation between no more than two authors is allowed. The prize cannot be divided among authors of different memoirs. If no memoir is received at the end of a period, this may be prolonged by the board of the academy for one year. If the prize is not awarded, the available amount will be added to the principal. Candidates are invited to send their work, typed in three copies, to the permanent secretary of the academy at the latest on Dec. 31 of the last year of the quadrennial period. For details apply to the secretary's office of the Royal Flemish Academy of Medicine of Belgium, Palace of the Academies, Hertogsstraat, 1, Brussels 1.

Meeting of Chest Physicians.—The American College of Chest Physicians will hold its five-day annual meeting in Miami Beach, with headquarters at the Saxony Hotel, June 8-12. Dr. Seymour M. Farber, San Francisco, president of the college, will preside. Among the topics to be discussed are "Newer Diagnostic Aids in Cardiology," "Cardiac Resuscitation," "Pulmonary Function in Cardiac Disease," "Carcinoma of the Lung: A Study of Five-Year Survivals Following Surgery," and "Effect of Cardiac Arrhythmias on the Circulation of the Vital Organs." A program of scientific motion pictures, to be presented June 10-12, has been arranged by Dr. Paul H. Holinger, of Chicago. Other highlights of the meeting will include the presentation of the college gold medal at the presidents' banquet on June 11 and the convocation at which 100 physicians will be awarded their certificates of fellowship in the college. The scientific program will include postgraduate seminars June 8. There will be two morning and two afternoon sessions devoted to cardiovascular and pulmonary discussions. The tuition fee of $7.50 for each postgraduate seminar will be included in the registration fee of $25 for nonmembers. Fireside conferences will be held on the evening of June 10, and a film presentation of a television broadcast, "Report to the People on Lung Cancer," is arranged. Six round-table luncheon discussions will be held daily, June 10-12. For information, write Mr. Murray Kornfeld, 112 E. Chestnut St., Chicago 11, Executive Director.

International Congress on Burns.—Scientists engaged in research in burns will meet at the National Naval Medical Center, Washington, D. C., Sept. 19-22 in the first International Congress on Research in Burns. The congress, sponsored by the U. S. Department of Defense, will be held at the School of Hospital Administration at the Naval Medical Center. More than 100 scientists—from Canada, Mexico, Chile, Peru, Scotland, England, Sweden, Yugoslavia, China, Italy, and the U. S. S. R. —will participate. Their fields of research include experimental as well as clinical aspects and touch on problems of skin grafts, immunology, metabolism, and surgery. The last conference on burns was held in October, 1955. Some 55 papers are scheduled to be given. At the close of each group of related papers, one scientist will summarize information on that phase of burns research. On the final day, six investigators will give their ideas on needed additional research. A volume on burns research is planned, to contain about 35 of the papers presented at the congress. Honorary chairman of the congress, being held under the auspices of the American Institute of Biological Sciences, is Dr. Frank D. Berry, assistant secretary of defense (health and medical). Congress co-ordinator is Dr. Curtis P. Artz, University of Mississippi Medical Center, Jackson, Miss.

Rheumatism Meeting in Florida.—The annual scientific sessions of the American Rheumatism Association will be held at the Hotel Diplomat, Convention Hall, Hollywood-by-the-Sea, Fla., June 9-11. The sessions open with a panel discussion June 9, 8 p. m., titled "Current Immunologic Research in Rheumatic Diseases—Possible Clinical Implications" and moderated by Dr. Lewis Thomas, professor of medicine, New York University Medical School. Concurrent sessions on experimental and pathologic observations are scheduled for June 10, 8:30 a. m. Thereafter, all sessions will be plenary. The presidential address by Dr. Charley J. Smyth, University of Colorado, Denver, will take place from 12:30 p. m., June 10. Dr. Smyth will present "Necrotizing Vasculitis, Mast Cells and Connective Tissue Diseases—An Hypothesis." Reports slated for June 11, 8:30 a. m. to noon, deal with rheumatic fever, the rheumatoid factor, and rheumatoid arthritis. The closing guest lecture will be given by Prof. E. G. L. Bywaters, of London, England, on clinical trials of gold salts conducted by the Empire Rheumatism Council's Research Subcommittee. In all, 46 scientific papers dealing with clinical and research findings in rheumatic diseases are included in the program. Following the meeting, a postgraduate seminar in arthritis and related diseases will take place at the Hotel Diplomat, sponsored by the Florida Chapter, Arthritis and Rheumatism Foundation, in cooperation with Florida medical societies and medical schools. For information, write Mr. Gerard W. Speyer, 10 Columbus Circle, New York 19, Executive Secretary.

Psychiatrists Plan World Tour.—The following papers will be presented by members of the Eastern Psychiatric Research Association during their world tour which starts July 1:

Role of Hypnosis in Psychiatry, Dr. Herbert X. Spiegel.
Newer Concepts of Feminine Personality, Dr. Natalie Shainess.
Electric and Chemical Convulsive Therapy in Psychiatry Today, Dr. David J. Impastato.
A Comparison of Pharmacotherapy and Electrotherapy, Dr. William Furst.
Recent Advances in Psychiatric Services to Courts and Prisons, Dr. Richmond C. Hubbard.
Responses to High Frequency Brain Stimulation in Psychiatric and Neurologic Diagnosis and Treatment, Dr. Alfred E. Eyres and Reuben Reiter, D.Sc.
Treatment of Emotional Factors in Learning Disability, Dr. Theodore Cohen.
Recent Advances in Psychiatric Training Programs in the United States, Dr. William L. Holt Jr.
Psychiatry in Relation to Medical Practice, Dr. Anthony R. Gabriel.
Pharmacotherapy of Depressive States, Dr. Francis A. Gagliardi.
Place of Insulin Coma Treatment Today, Dr. Edwin M. N. Dunlop.
Place Today of Regressive Convulsive Therapy and Lobotomy in the Treatment of Mental Disorders, Dr. James L. Sagebiel.
Present Role of Somatic and Analytic Treatment in Child Psychiatry, Dr. Herbert Freed.

These meetings will be held in conjunction with the psychiatric societies of Japan, Thailand, Hong Kong, India, and Israel. The association has engaged the University Travel Company, 18 Brattle St., Cambridge, Mass., to handle all the traveling arrangements for them. Anyone interested in joining the tour can do so by contacting Mr. C. J. Johns, of the University Travel Company.

FOREIGN

Rheumatology Congress in Czechoslovakia.—The Czechoslovak Society of Physical Medicine is holding the Czechoslovak Congress of Rheumatology with international participation Sept. 21-25 in Piestany. Two main subjects will form the principal part of the program: "Rheumatoid Arthritis" and "Ochronotic Arthropathy." Subjects of free choice are planned, and papers will be read by researchers from Bulgaria, Denmark, Finland, France, Germany, Great Britain, Hungary, Italy, Norway, Poland, Rumania, Soviet Union, Sweden, U. S. A., and Czechoslovakia. The official languages of the congress are English, French, Russian, German, Czech, and Slovak. Simultaneous translation to and from the official languages will be provided. Excursions and social and cultural functions are planned, and a special program is being prepared for the accompanying family members. For information, write the Secretariat of the Czechoslovak Congress of Rheumatology, Praha 2, Na slupi 4, Czechoslovakia.

CORRECTIONS

Common Colds.—In the letter from the United Kingdom on common colds (April 23, page 1970), the report referred to was by D. A. J. Tyrrell and co-workers and appeared in *The Lancet* for Jan. 30.

Dr. Barth Heads Radiologists.—In a Medical News item on page 66 of the May 7 Journal, concerning the awarding of gold medals by the American College of Radiology, the fact that Dr. Earl E. Barth, Chicago, is the newly elected president of the college was inadvertently left out.

EXAMINATIONS AND LICENSURE

EDUCATIONAL COUNCIL FOR FOREIGN MEDICAL GRADUATES, INC.

Educational Council for Foreign Medical Graduates: Stations around the world. Sept. 21, 1960. Exec. Director, Dr. Dean F. Smiley, 1710 Orrington Ave., Evanston, Ill.

NATIONAL BOARD OF MEDICAL EXAMINERS

National Board of Medical Examiners: Part I, Various Cities, June 21-22 and Sept. 7-8. Part II. Applications must be received at least six weeks before the date of the examination. Exec. Sec., Dr. John P. Hubbard, 133 South 36th St., Philadelphia.

BOARDS OF MEDICAL EXAMINERS

Alabama: *Examination.* Montgomery, June 21-23. Sec., Dr. D. G. Gill, State Office Bldg., Montgomery.

Alaska:* On application in Anchorage or Fairbanks. Sec., Dr. W. M. Whitehead, 172 South Franklin St., Juneau.

Arkansas:* *Examination and Reciprocity.* Little Rock, June 9-10 Sec., Dr. Joe Verser, Harrisburg.

California: *Written.* San Francisco, June 20-23; Los Angeles, Aug. 22-25 and Sacramento, Oct. 17-20. *Oral and Clinical.* Los Angeles, San Francisco, June 19; Los Angeles, Aug. 21, and Los Angeles, Nov. 29. *Oral for Reciprocity Applicants.* San Francisco, June 18; Los Angeles, Aug. 20 and Nov. 19. Sec., Dr. Louis E. Jones, Room 536, 1020 N Street, Sacramento.

Canal Zone: On Application. Acting Sec., Dr. B. K. Levin, Health Bureau, Balboa Heights.

Colorado:* *Examination.* Denver, June 14-15. Sec., Dr. John B. Farley, 1612 Tremont Place, Denver 2.

Connecticut:* Hartford, July 13-14. Sec., Dr. Stanley B. Weld, 160 St. Ronan St., New Haven.

Delaware: *Examination and Endorsement.* Dover, June 12-14 and July 21. Sec., Dr. Joseph S. McDaniel, Professional Bldg., Dover.

District of Columbia:* *Examination.* Washington, June 13-14. Deputy Director, Mr. Paul Foley, Department of Occupations and Professions, 1740 Massachusetts Ave., N.W., Washington 6.

Florida:* *Examination.* Miami Beach, June 19-21. Sec., Dr. Homer L. Pearson, 901 N.W. 17th St., Miami 36.

Georgia: *Examination.* Atlanta and Augusta, June 8-9. *Reciprocity.* Atlanta and Augusta, June 10. Sec., Mr. Cecil L. Clifton, 224 State Capitol, Atlanta 3.

Guam: *Subject to Call.* Act Sec., Dr. F. L. Conklin, Agana.

Idaho: *Examination and Endorsement.* Boise, July 11-13. Exec. Sec., Mr. Armand L. Bird, 358 Sonna Bldg., Boise.

Indiana: *Examination.* Indianapolis, June 22-24. *Reciprocity.* Indianapolis, fourth Wednesday of each month. Ex. Sec., Miss Ruth V. Kirk, 538 K. of P. Bldg., Indianapolis.

Illinois: *Examination.* Chicago, July 12-14. *Reciprocity.* Chicago, July 15. Supt. of Registration, Mr. Frederic B. Selcke, Capitol Bldg., Springfield.

Kansas:* *Examination.* Kansas City, June 16-17. *Endorsement.* Kansas City, June 18. Sec., Dr. F. J. Nash, New Brotherhood Bldg., Kansas City.

Kentucky: *Examination.* Louisville, June 6-7. Sec., Dr. Russell E. Teague, 620 South Third St., Louisville 2.

Louisiana: *Examination and Reciprocity.* New Orleans, June 9-11. Sec., Dr. Edwin H. Lawson, 930 Hibernia Bank Bldg., New Orleans 12. *Homeopathic.* Examination subject to call. Sec., Dr. F. H. Hardenstein, 903 Pere Marquette Bldg., New Orleans.

Maryland: *Examination.* Baltimore, June 15-18. Sec., Dr. Frank K. Morris, 1215 Cathedral St., Baltimore 1.

Massachusetts: *Examination.* Boston, July 12-15. Sec., Dr. David W. Wallwork, Room 37, State House, Boston 33.

Michigan:* *Examination.* Ann Arbor and Detroit, June 6-8. Sec., Dr. E. C. Swanson, 118 Stevens T Mason Bldg., Lansing.

Mississippi: *Examination.* Jackson, June 20-21; *Reciprocity,* Jackson, June 16. Sec., Dr. A. L. Gray, Old Capitol, Jackson 13.

Montana: *Examination and Reciprocity.* Helena, Oct. 4. Sec., Dr. Thomas L. Hawkins, 555 Fuller Ave., Helena.

Nebraska:* *Examination.* Omaha, June 13-15, 1960. Dir., Bureau of Examining Boards, Room 1009, State Capitol Bldg., Lincoln 9.

Nevada: *Examination and Reciprocity.* Reno, June 8, Sept. 7 and Dec. 7. Sec., Dr. G. H. Ross, 112 North Curry St., Carson City.

New Hampshire: *Examination and Reciprocity.* Concord, Sept. 14-17. Sec., Dr. Edward W. Colby, 61 South Spring St., Concord.

New Jersey: *Examination.* Trenton, June 21-24. *Reciprocity.* Continuously. Sec., Dr. Royal A. Schaaf, 28 West State St., Trenton.

New York: *Examination.* Albany, Buffalo, New York City, Rochester and Syracuse, June 28-July 1. Sec., Dr. Stiles D. Ezell, 23 S. Pearl Street, Albany.

North Carolina: *Examination and Endorsement.* Raleigh, June 20-23. Sec., Dr. Joseph J. Combs, 716 Professional Bldg., Raleigh.

North Dakota: *Examination and Reciprocity.* Grand Forks, July 13-16. Sec., Dr. C. J. Glaspel, Grafton.

Ohio: *Reciprocity.* Columbus, June 17. *Examination.* Columbus, June 16-18. Sec., Dr. H. M. Platter, 21 West Broad St., Columbus 15.

Oklahoma:* *Examination and Endorsement.* Oklahoma City, May 31-June 1. Sec., Dr. E. F. Lester, 813 Braniff Bldg., Oklahoma City.

Oregon:* *Examination.* Portland, July 12-13, Exec. Sec., Mr. Howard I. Bobbitt, 609 Failing Bldg., Portland.

Pennsylvania: *Examination.* Philadelphia and Pittsburgh, July 5-7. Sec., Mrs. Margaret G. Steiner, Box 911, Harrisburg.

Rhode Island:* *Reciprocity.* Providence, June 23. *Examination.* Providence, July 7-8. Administrator, Mr. Thomas B. Casey, 366 State Office Bldg., Providence.

South Carolina: *Examination.* Columbia, June 28-29. Sec., Dr. Harold E. Jervey, Jr., 1329 Blanding St., Columbia.

South Dakota:* *Examination.* Rapid City, July 19-20. *Reciprocity.* Continuously. Exec. Sec., Mr. John C. Foster, 300 First National Bank Bldg., Sioux Falls.

Tennessee:* *Examination.* Nashville, May 31-June 1; Memphis, June 15-16. *Reciprocity.* Continuously. Sec., Dr. Alfred H. Mason, 1635 Exchange Bldg., Memphis 3.

Texas:* *Examination and Reciprocity.* Fort Worth, June 20-22. Sec., Dr. M. H. Crabb, 1714 Medical Arts Bldg., Fort Worth 2.

Utah: *Examination.* Salt Lake City, July 6-8. Director, Mr. Frank E. Lees, 324 State Office Bldg., Salt Lake City 1.

Vermont: *Examination and Reciprocity.* Burlington, June 16-18. Sec., Dr. F. J. Lawliss, Richford.

Virgin Islands: *Examination.* Charlotte Amalie, St. Thomas, June 8-9. Sec., Dr. Benjamin A. Nath, Charlotte Amalie, St. Thomas.

Virginia: *Examination and Reciprocity.* Richmond, June 13-17. Address: Board of Medical Examiners, 631 First St. S.W., Roanoke.

Washington:* *Examination.* Seattle, July 18-20. *Reciprocity.* Continuously. Administration, Mr. Thomas A. Carter, Capitol Bldg., Olympia.

Wisconsin:* *Examination.* Milwaukee, July 12-14. Sec., Dr. Thomas W. Tormey, 115 So. Pickney St., Madison.

Wyoming: *Examination and Reciprocity.* Cheyenne, June 6. Acting Sec., Dr. Carleton D. Anton, State Office Bldg., Cheyenne.

BOARDS OF EXAMINERS IN THE BASIC SCIENCES

Alabama: *Examination.* Birmingham, June 2-3. *Waiver.* Continuously. Final date for acceptance of applications for examination is May 18 and for waiver May 6. Chairman, Dr. E. Carl Sensenig, 1919 7th Ave., So., Birmingham 3.

Arizona: *Examination.* Tucson, June 21. *Reciprocity.* Tucson, Approximately June 25. Sec., Mr. Hirman E. Bateman, University of Arizona, Tucson.

Colorado: *Examination and Reciprocity.* Denver, Sept. 7-8 and Dec. 7-8. Sec., Dr. Esther B. Starks, 1459 Ogden St., Denver 18.

Connecticut: *Examination.* New Haven, June 11. *Reciprocity and Endorsement.* Continuously. Exec. Asst., Mrs. Regina G. Brown, 258 Bradley St., New Haven 10.

District of Columbia: *Examination.* Washington, May 23-24. Deputy Director, Mr. Paul Foley, Department of Occupations and Professions, 1740 Massachusetts Ave., Washington 6.

Florida: *Examination.* Miami, June 4. Sec., Mr. M. W. Emmel, Box 340, Gainesville.

Kansas: *Examination.* Kansas City, June 10-12. Sec., Dr. Leon C. Heckert, Kansas State College, Pittsburg.

Minnesota: *Examination.* Minneapolis, June 7-8. *Reciprocity. Continuously.* Sec., Dr. Raymond N. Beiter, 105 Millard Hall, University of Minnesota, Minneapolis 14.

New Mexico: *Reciprocity.* Santa Fe, June 25. *Examination.* Santa Fe, July 17. Sec., Mrs. Marguerite Cantrell, Box 1522, Santa Fe.

Oregon: *Examination.* Portland, June 4. *Reciprocity.* Continuously. Sec., Dr. Earl M. Pallett, Box 5175, Eugene.

South Dakota: *Examination and Reciprocity.* Vermillion, June 10-11. Sec., Dr. Gregg M. Evans, 310 E. 15th St., Yankton.

Washington: *Examination.* Seattle, July 13-14. Administrator, Mr. Thomas A. Carter, Department of Licenses, Capitol Bldg., Olympia.

Wisconsin: *Examination.* Milwaukee, June 4. Sec., Dr. W. H. Barber, 621 Ransom St., Ripon.

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*Basic Science Certificate required.

GOVERNMENT SERVICES

NAVY

Personal.—Rear Adm. Frank P. Kreuz, M. C., U. S. N., former deputy commanding officer of the National Naval Medical Center and commanding officer of the U. S. Naval Hospital, Bethesda, Md., became the 18th commanding officer of the center in ceremonies on March 31. He relieved Rear Adm. Bruce E. Bradley, M. C., U. S. N., who retired after over 33 years of active duty.

VETERANS ADMINISTRATION

Night Care for Mental Patients.—When quitting time comes at shops and offices across the nation these days, a sizable group of workers collect their belongings and head for the wards of Veterans Administration psychiatric hospitals. These veterans in the final phase of recovery from mental illness spend the night at the hospitals, where they receive drugs or other treatment, and the next morning receive a pass from the hospital and leave for another day's work. They are showing definite benefit from this program.

Dr. Jesse F. Casey, VA director of the psychiatry and neurology service, explained that many patients, long hospitalized for mental illness, require additional help after specific therapy has been given. They cannot make an abrupt change from hospital to community life. Receiving night care for a limited time often enables them to leave the hospital and return home. They reach this phase of the program only after months or years of treatment, vocational counseling, and participation in therapeutic work assignments at the hospitals. Retention in the program is generally limited to a year and often is much less than that. These patients achieve excellent work records and a large percentage recover and leave the hospital. Much of the credit for the success of the night care program belongs to employers in communities where VA hospitals are located.

PUBLIC HEALTH SERVICE

Staff Changes.—Surgeon General Leroy E. Burney of the Public Health Service announced three key staff changes which will become effective July 1. Dr. David E. Price, now chief of the bureau of state services, will become deputy director of the National Institutes of Health, a position which has been vacant since the retirement of Dr. Cassius J. Van Slyke last December. Dr. Theodore J. Bauer, present deputy chief of the bureau of state services, will succeed Dr. Price as bureau chief. Dr. Kenneth M. Endicott, now an associate director of the National Institutes of Health, will be director of the National Cancer Institute, succeeding Dr. John R. Heller, who has been granted leave by the service to accept the presidency of the Sloan-Kettering Memorial Cancer Center in New York City. No successor has as yet been selected for Dr. Bauer's present post.

DEPARTMENT OF COMMERCE

Russian Literature on Air Pollution.—A survey of U. S. S. R. literature on air pollution and related occupational diseases is being conducted by Dr. Ben S. Levine under a U. S. Public Health Service research grant. The first volume in the survey was released for sale to the public by the Office of Technical Services, Business and Defense Services Administration, U. S. Department of Commerce. Doctor Levine's survey is primarily for the benefit of the English-speaking scientist who wants information on Russian air pollution research. The survey covers the basic concepts of air pollution prevention in the U. S. S. R., explains the methods of approach, outlines the scope and plan of the work, and evaluates the progress made.

Previous volumes of Russian air pollution studies condensed and translated by Doctor Levine for the U. S. Public Health Service include, "Sanitary Protection of Atmospheric Air—Purification of Industrial Discharge Gases from Suspended Substances" (OTS 59-21092) and "Limits of Allowable Concentrations of Atmospheric Pollutants" (book 1—OTS 59-21173, book 2—OTS 59-21174, book 3—OTS 59-21175).

The initial volume of the newest survey series is "U. S. S. R. Literature on Air Pollution and Related Occupational Diseases," volume 1, B. S. Levine, Ph.D., U. S. Public Health Service, Department of Health, Education, and Welfare research grantee, January, 1960, 214 pages (order OTS 60-21049 from OTS, U. S. Department of Commerce, Washington 25, D. C., $3.50). This is the first volume in a series of survey reports to be completed under a U. S. Public Health Service research grant. The volume contains 38 condensed translations and supplements of Russian literature on air pollution and related occupational diseases. The survey is being conducted primarily for the information of non-Russian scientists who are interested in reports on air pollution research and antipollution progress in the U. S. S. R. The reports and supplements in volume 1 are grouped in three categories: (1) general information, (2) studies of toxicity and its effect on health and general living conditions, and (3) analytic findings. All information is factually presented and is based on experimental research data developed in the same manner as in other countries.

DEATHS

Atwood, Alton Curtis, Modesto, Calif.; College of Medical Evangelists, Loma Linda and Los Angeles, 1925; veteran of World War I; served as health officer of Chowchilla; associated with the Modesto State Hospital; died in the Memorial Hospital March 25, aged 62, of a heart attack.

Barker, Creighton Ⓜ for 22 years executive secretary of the Connecticut State Medical Society, died at his home in Hamden, Conn., April 8, aged 68, of ruptured aneurysm. Dr. Barker was born in New Milford, Conn., Jan. 15, 1892. He received his early education in New Milford schools, and graduated from Dartmouth College in 1910, and from Dartmouth Medical School in Hanover, N. H., in 1913. He interned at New Haven Hospital and then enlisted in the medical corps of the U. S. Army, serving in France during World War I. Upon his return he entered private practice in New Haven and served as associate clinical professor of otolaryngology at Yale University School of Medicine. He was a specialist certified by the American Board of Otolaryngology. From 1936 until his retirement in 1958, he was executive secretary of the Connecticut State Medical Society and in 1956 a new conference room of the society was named in his honor, in recognition of his long service. He was secretary of the Connecticut Medical Examining Board from 1941 to 1948. Prior to his retirement, Dr. Barker was vice-president of the National Board of Medical Examiners, member of the National Committee on Chronic Illness, the National Committee on Evaluation and Foreign Medical Credentials, and the board of directors of the Connecticut Medical Service, chairman of the Connecticut State Advisory Committee to the Selective Service System, and a member of the National Advisory Board for Medical Specialties. From 1944 to 1954 he was a member of the House of Delegates of the American Medical Association and in 1948 and 1949 an alternate delegate from the American Medical Association to the World Medical Association. During World War II he was consultant for the Procurement and Assignment Service for Physicians War Manpower Committee, Washington, D. C. He was a member of the Connecticut Veterans Advisory Committee, the board of trustees of the University of Connecticut, Storrs, and the board of directors of Connecticut Blue Cross. In August, 1949, he attended the first World Conference on Medical Education in London as a representative of the Federated Medical Examining Boards of the United States, of which he was past-president. Dr. Barker was past-president of the Connecticut Cancer Society, and received the 1955 medal for distinguished service in cancer control, the highest annual award of the Connecticut division of the American Cancer Society, of which he was also past-president.

Beckman, John Cornelius, Daytona Beach, Fla.; Medical College of the State of South Carolina, Charleston, 1909; also a graduate in pharmacy; in 1939 was honored by the Metropolitan Life Insurance Company on the occasion of his 25th anniversary as medical examiner in the Charleston, S. C., district; died March 19, aged 75, of influenza.

Bottorff, Charles M., Charlestown, Ind.; Kentucky School of Medicine, Louisville, 1888; died in Louisville, Ky., March 26, aged 99, of uremia.

Brandon, Thomas Campbell Ⓜ San Jose, Calif.; Jefferson Medical College of Philadelphia, 1935; interned at the Williamsport (Pa.) Hospital; veteran of World War II and won the Legion of Merit; associated with O'Connor and Doctors hospitals; served on the staff of a clinic in Anchorage, Alaska, and as chief surgeon of the Alaska Railway; died in Spotswood Memorial Hospital, Los Gatos, March 29, aged 50, of cirrhosis of the liver.

Brickwede, John Louis Ⓜ Akron, Ohio; Western Reserve University School of Medicine, Cleveland, 1914; member of the American Academy of General Practice; on the staffs of Akron City, Akron General, and Children's hospitals; died in Salem (Ohio) City Hospital March 22, aged 75, of arteriosclerotic heart disease.

Brown, William Thomas Jr. Ⓜ Laurinburg, N. C.; Northwestern University Medical School, Chicago, 1946; interned at the Harper Hospital in Detroit; served a residency at the White Cross Hospital in Columbus, Ohio, and the North Carolina Memorial Hospital in Chapel Hill; from 1946 to 1948 an officer in the Medical Corps, Army of the United States; associated with the Scotland County Memorial Hospital, where he died March 29, aged 39, of periarteritis nodosa.

Buckborough, Morris Webster Ⓜ South Haven, Mich.; University of Michigan Medical School, Ann Arbor, 1932; member of the American Academy of General Practice; served as president of the Van Buren County Medical Society; chief of staff of the South Haven Hospital; member of the Chamber of Commerce; died in Kalamazoo March 25, aged 56.

Ⓜ Indicates Member of the American Medical Association.

Chapin, Clarence D. Ⓜ Columbiaville, Mich.; Detroit College of Medicine, 1904; veteran of World War I; served on the school board; died March 20, aged 80, of ruptured aortic aneurysm.

Christensen, Eugene Leslie Ⓜ Los Angeles; University of Minnesota Medical School, Minneapolis, 1924; specialist certified by the American Board of Ophthalmology; fellow of the American Academy of Ophthalmology and Otolaryngology; member of the Los Angeles Society of Ophthalmology and Otolaryngology; senior attending surgeon at the Lutheran Hospital; died March 22, aged 61.

Packard, Rollo Kirk, Los Angeles; born in Rockford, Mich., July 22, 1886; Chicago College of Medicine and Surgery, 1911; served on the faculty of his alma mater; past-president of the Illinois State Medical Society and served as chairman and member of its council; for many years member of the council of the Chicago Medical Society; member of the House of Delegates of the American Medical Association from 1938 to 1944, from 1946 to 1948, and in 1950; served as president of the Blue Shield, Chicago, and as vice-president of the Chicago Blue Cross; fellow of the International College of Surgeons and the American College of Surgeons; veteran of World War I; served as chairman of the hospital board, chief of staff, and president of the board of directors, Woodlawn Hospital in Chicago; died March 28, aged 73, of cardiac infarction.

Pearce, John Musser, New York City; born in New York City Oct. 23, 1908; Harvard Medical School, Boston, 1934; certified by the National Board of Medical Examiners; specialist certified by the American Board of Pathology; member of the American Association of Pathologists and Bacteriologists, College of American Pathologists, and the American Society for Experimental Pathology; served on the staff of the Rockefeller Institute for Medical Research, Princeton, N. J.; professor of pathology and pathologic surgeon at Cornell University Medical College; formerly on the faculty of Long Island College of Medicine in Brooklyn; associated with the New York Hospital; served on the staffs of the Sloane Hospital for Women and the Presbyterian Hospital in New York City, Long Island College Hospital in Brooklyn, and the Mary Immaculate Hospital in Jamaica; aged 51, drowned March 22, while bathing at Sanibel Island, Fort Myers, Fla.

Peterson, Charles A. Ⓜ Spruce Pine, N. C.; North Carolina Medical College, Charlotte, 1907; served as Mitchell County legislator, mayor of Spruce Pine, and president of the Chamber of Commerce; formerly director and chairman of the board of managers of Northwestern Bank of Spruce Pine; died in Fort Myers, Fla., March 14, aged 77, of a hip fracture received in a fall.

Purves, Arthur Matthew, Des Plaines, Ill.; Bennett Medical College, Chicago, 1901; for many years on the board of health, president of the grammar school board, Maine Township school trustee, and on the Maine Township High School Board; a director of the First National Bank of Des Plaines and served as chairman of the First Federal Savings and Loan Association; associated with Augustana and St. Mary's of Nazareth hospitals in Chicago; died April 2, aged 83, of a heart attack.

Rau, Gerald Albert Ⓜ Manitowoc, Wis.; University of Wisconsin Medical School, Madison, 1929; served as county coroner; past-president of the Manitowoc County Medical Society; veteran of World War II; died in the Holy Family Hospital March 18, aged 55.

Ray, Roy Williams Jr., Charleston, S. C.; Medical College of Georgia, Augusta, 1953; interned at Macon Hospital in Macon, Ga.; served a residency at the Baroness Erlanger Hospital in Chattanooga, Tenn., and the Medical Center Hospitals in Charleston; died Feb. 11, aged 32.

Reser, Thomas S. Ⓜ Cole Camp, Mo.; Barnes Medical College, St. Louis, 1907; died in the Bothwell Hospital, Sedalia, March 17, aged 78.

Rhudy, William Porter, Penn Yan, N. Y.; Indiana University School of Medicine, Indianapolis, 1924; member of the American Academy of General Practice; awarded the Bronze Star for conspicuous and meritorious service during World War II; formerly associated with the Clifton Springs (N. Y.) Sanitarium; died March 17, aged 60.

Ridenour, Joseph Elmer, Waterloo, Iowa; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1901; formerly city health officer; associated with Allen Memorial, St. Francis, and Schoitz Memorial hospitals; died March 11, aged 86, of bronchiectasis.

Rosenfeld, Joseph Ehrlich, Battle Creek, Mich.; McGill University Faculty of Medicine, Montreal, Que., Canada, 1922; fellow of the American College of Surgeons; member of the Industrial Medical Association; died in the Henry Ford Hospital, Detroit, April 2, aged 61, of leukemia.

Rowley, Walter Nelson, Huntington, W. Va.; Northwestern University Medical School, Chicago, 1918; fellow of the American College of Surgeons; came to the Mayo Clinic, Rochester, Minn., in 1919, as associate in the section on obstetrics and left Jan. 1, 1923; veteran of World War I; for many years active in the U. S. Naval Reserve and was released with the rank of lieutenant commander;

owner of the Rowley Clinic Hospital; served on the staff of St. Mary's Hospital; died March 19, aged 66, of acute cerebral thrombosis.

Sabol, John Gregory Ⓜ Philadelphia; University of Pennsylvania School of Medicine, Philadelphia, 1921; associated with the Doctors Hospital; for many years on the staff of St. Mary's Hospital, where he died March 23, aged 66.

Salzman, Nathan Ⓜ Paterson, N. J.; University and Bellevue Hospital Medical College, New York City, 1920; for many years chief radiologist at Barnert Memorial Hospital; served on the staff of Beth Israel Hospital in Passaic; died March 16, aged 66.

Sharp, Cyrus Kosciusko Ⓜ Arlington, Ga.; Louisville (Ky.) Medical College, 1898; member of the House of Delegates of the American Medical Association in 1946, 1948, and 1949; past-president of the Medical Association of Georgia; for many years served on the state board of health; in 1952 named "Practitioner of the Year in the State of Georgia"; died March 12, aged 92.

Sharpe, William, St. Petersburg, Fla.; Harvard Medical School, Boston, 1908; fellow of the American College of Surgeons; for many years practiced in New York City, where he was associated with the Beekman-Downtown, Roosevelt, Gouveneur, and Manhattan General hospitals; author of an autobiography published in 1952 entitled "Brain Surgeon"; died March 29, aged 77, of cerebral thrombosis.

Spencer, Aleck, Abilene, Texas; Louisville (Ky.) Medical College, 1904; served as a member of the staff of the New Mexico State Hospital in Las Vegas, N. M., and the Austin (Texas) State Hospital; died March 18, aged 77.

Stewart, Edgar Allen, St. Petersburg, Fla.; State University of Iowa College of Medicine, Iowa City, 1912; veteran of World War I; retired from the Veterans Administration on May 29, 1951; died March 15, aged 78, of carcinoma of the prostate with multiple metastases.

Strongman, Bessie Talbot, Los Angeles; Johns Hopkins University School of Medicine, Baltimore, 1919; volunteered as a medical relief worker for the American Friends Commission and was head of a settlement house clinic in Marseilles, France; at one time associated with the E. I. Du Pont de Nemours Company in Charlestown, Ind.; served as resident physician at the G. N. Wilcox Memorial Hospital in Lihue, Kauai, Hawaii; died Feb. 23, aged 68, of coronary occlusion.

Supernaw, Jack Shores, Madison, Wis.; University of Wisconsin Medical School, Madison, 1927; fellow of the American College of Surgeons; past-president of the Dane County Medical Society; served on the board of education; associated with the Madison General Hospital; died March 2, aged 60.

Sweet, Ossian Haven, Detroit; Howard University College of Medicine, Washington, D. C., 1921; veteran of World War I; died March 19, aged 65.

Tranter, Paul Webster, Chicago; University of Illinois College of Medicine, Chicago, 1924; member of the staff of the Walther Memorial Hospital; died March 26, aged 72, of coronary occlusion.

Van Kirk, John Albert Ⓜ Frankfort, Ind.; University of Illinois College of Medicine, Chicago, 1914; past-president of the Clinton County Medical Society; past-president of the Ninth District of the Indiana State Medical Association; veteran of World War I; past-president of the staff of the Clinton County Hospital, where he died March 19, aged 69.

Walker, Harold Layton Ⓜ Elmira, N. Y.; born in Buffalo Nov. 1, 1908; University of Buffalo School of Medicine, 1932; interned at the Buffalo General Hospital, where he served a residency; served a residency at the Children's Hospital and the Buffalo City Hospital; specialist certified by the American Board of Dermatology; member of the American Academy of Dermatology and Syphilology; certified by the National Board of Medical Examiners; past-secretary of the Chemung County Medical Society; veteran of World War II; associated with the St. Joseph's Hospital and Arnot-Ogden Hospital, where he died March 13, aged 51.

Webber, Millard Carroll Ⓜ Portland, Maine; Medical School of Maine, Portland, 1910; veteran of World War I; on the staffs of the Maine Medical Center and Mercy Hospital; died March 19, aged 77, of pneumonia.

Wiedman, Earl Vernon Ⓜ Lincoln, Neb.; University of Nebraska College of Medicine, Omaha, 1919; member of the American Academy of General Practice; on the staffs of the Bryan Memorial and St. Elizabeth Hospital; medical director of Nebraska National Life Insurance Company; died March 18, aged 67, of cerebral hemorrhage.

Young, Cuthbert Ben Ⓜ Tyler, Texas; University of Minnesota Medical School, Minneapolis, 1937; interned at the Minneapolis General Hospital; past-president of the Smith County Medical Society; member of the American College of Chest Physicians; served on the school board; for five years school physician; staff physician at the Mother Frances and Medical Center hospitals; consulting physician at the East Texas Tuberculosis Hospital; recipient of the district service award of the Junior Chamber of Commerce; died March 17, aged 52.

FOREIGN LETTERS

AUSTRIA

Human Milk.—At the meeting of the Society of Pediatrics in Vienna in February Dr. H. O. Juergenssen said that the human milk center of Vienna had increased its yearly collection of human milk to 15,000 liters. While most of the milk was sterilized by means of heat and was kept in liquid form, 4.5 liters had been lyophilized daily for several months. This is the best method of preservation because it retains the raw character of the milk almost entirely. The powdered milk can be stored at room temperature for months. Lyophilization and subsequent storage reduce the bacterial count as effectively as pasteurization.

FRANCE

Leptospirosis.—B. Kolochine-Erber and co-workers (*Presse méd.* 67:2089, 1959) said that, although infection with Leptospira australis had been recognized for a long time in cattle and horses, such an infection was not detected in man in France until 1952. Because the disease in man is always mild, the clinician usually feels no urge to make serologic tests. Since 1952 growing interest in the disease, which is most prevalent in summer and autumn, has led to the discovery that the disease is commoner than was supposed.

Carbon Monoxide Poisoning.—L. Binet and co-workers (*Presse méd.* 67:2125, 1959) stated that carbon monoxide poisoning is relatively common and the patient fatality rate is about 15.7%. In severe cases artificial hibernation is the most effective treatment, except when an associated barbiturate poisoning cannot be ruled out. They used this therapy in six comatose patients, and of these three died and three were completely cured. They believe that hibernation should be used in all severe cases immediately after first aid has been administered.

GERMANY

Vitamin B_{12} Therapy.—E. Hiller and S. Wallner of Munich (*Deutsches med. J.* 10:399, 1959) stated that the effect of vitamin B_{12} on the hematopoietic system has been long established and led to its use in the treatment of pernicious anemia and other chronic anemias. This vitamin also has a favorable effect in many other diseases. The mechanism of its action is not fully understood. It increases sugar absorption in patients with adrenal cortical hypofunction. Blood cholesterol levels decline and, therefore, a favorable effect on arteriosclerosis may occur. Vitamin B_{12} apparently takes part in protein synthesis. Its absorption is decreased in diabetes. A number of diseases such as hyperthyroidism are associated with increased requirements for the vitamin. A deficiency of the vitamin may be expected in hyperthyroidism and diabetes of long standing, and patients with these conditions should be given vitamin B_{12}.

The authors gave a series of 110 patients with various diseases each 1,000 mcg. of vitamin B_{12} daily. In this series 32 patients with hyperthyroidism were markedly improved in their general condition. In many of them the elevated metabolic rate decreased without further treatment and they gained weight. In the patients whose basal metabolic rate was increased by 80 to 100% no decrease in this rate was achieved. Twenty-one patients with gastrointestinal disorders were subjectively improved and also gained up to 1 kg. in body weight in the first week. In a woman with hyperemesis gravidarum vomiting completely ceased after four injections, and she gained some weight, but a second woman with this disease did not respond to the treatment. Six patients who had difficulty in recovering from an infection were improved. Ten patients with neuritis and neuralgia reported a decrease of pain, but doses up to 40,000 mcg. were required. Four patients with ischalgia, three with facial neuralgia, and two with migraine responded well.

Virtually no effect was obtained in severe neuritis, rheumatic facial paresis, acute polyarthritis, neurasthenia, psychopathy, or multiple sclerosis. A woman with persistent labyrinthine hydrops was markedly improved, and the result was amazing in a patient with ulcerative colitis and bronchial asthma. Not only were the allergic symptoms improved but the patient also gained weight. A patient with a treatment-resistant case of aphthous stomatitis was cured by 15 injections and simultaneous administration of a broad-spectrum antibiotic.

Adrenocortical Hormones and the Surgical Patient.—J. Rehn of Freiburg University (*Bruns' Beitr. klin. Chir.* 198:154, 1959) stated that although the indications for the adrenal cortical hormones have been defined these hormones (in particular prednisone and prednisolone) are used in ever-increasing extent due to the numerous scientific reports and the intensive advertising of pharmaceutical

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The items in these letters are contributed by regular correspondents in the various foreign countries.

firms. They are often used regardless of, or in ignorance of, their side-effects and then give rise to serious conditions. Their anti-inflammatory effect, which has achieved surprising results in rheumatic diseases, may cause extensive propagation of a suppurative infection. Local injections of hydrocortisone may give rise to similar complications. A major point is that local and general treatment, by reducing resistance to infective organisms, may lead to mistaking phlegmons for rheumatic diseases. These hormones should, therefore, be given only when the diagnosis has been clearly established.

A well-known side-effect is activation of tuberculosis. Dangerous complications may originate from the inhibition of inflammatory processes and the simultaneous suppression of the reaction of connective tissue in the gastrointestinal tract. In one case perforation of the large intestine was observed in a patient with ulcerative colitis after 1.5 Gm. of cortisone had been given. Existing, including already healing, peptic ulcers also may be activated. Hormone treatment after surgical gastrointestinal anastomosis increases the danger of dehiscence of the suture due to suppression of scar formation. The adrenocortical hormones are definitely contraindicated in such surgical infections as paronychia, phlegmon, and osteomyelitis, while they are justifiable in such cases as severe burns and peritonitis after these have been surgically treated and the genesis is perfectly clear. Simultaneous administration of large doses of an antibiotic is necessary.

Tuberculosis in Children.—H. Hartl (*Thoraxchirurgie* 7:51, 1959) said that, since pulmonary tuberculosis in childhood differs in its form and course from the disease in adults, the firmly established indications for surgical treatment in adults cannot be applied indiscriminately to children. The main prerequisite for successful treatment is close cooperation between chest physician and surgeon. Localized lesions of long standing are the main indication for operation. In primary tuberculosis in children, frequent as it is, with swellings of hilar lymph nodes, the numerous possible complications (lobular and segmental atelectases) can be prevented by endobronchial measures with appropriately conservative treatment. The respiratory passages are freed by aspiration that is controlled through the bronchoscope and by measures to counteract the mucosal swelling. Lymph nodes that have penetrated in the bronchus also are removed by aspiration or with biopsy forceps, which usually renders transthoracic excision of the mediastinal lymph nodes superfluous.

A series of 86 children were successfully treated with repeated bronchoscopy (under anesthesia and with supplemental oxygen). In addition to the indications for lung resection in adults (lung destruction, tuberculosis of the large bronchi, poststenotic bronchiectases, residual cavities after collapse therapy, and giant cavities), the primary caseous cavity focus which has already broadly invaded the bronchus is a further indication in children, as it does not respond to conservative measures. In this series segmental resection was performed in six children and lobectomy in nine. There were no deaths. Postoperative dissemination occurred in one patient but was controlled. Collapse treatment is becoming rare in children, but resections are increasing. The main reasons for this are greater plasticity of the child's thorax, good expansion of the residual lung without emphysema, and absence of complications in the bronchial stump. Resection, in the presence of appropriate indications, gives satisfactory results. Thoracoplasty in childhood is, therefore, no longer justifiable.

Renal Tuberculosis.—H. Junge (*Med. Klin.* 54:29, 1959) stated that 80 to 90% of renal tuberculosis is accompanied by chronic cystitis, even though the bladder contains no tubercles. The micro-organisms normally present in the bladder are usually absent. Patients between 20 and 40 years of age are predisposed to renal tuberculosis when they have skeletal tuberculosis. Retrograde pyelography is likely to spread the tuberculous process and it should, therefore, be used with caution. Urogenital tuberculosis occurs within four to eight years of other specific organic affections. It has a much longer latent period than osseous tuberculosis (one to three years) and does not result from this, but both originate from the same primary focus at the same time. The bilateral beginning of primary cortical renal tuberculosis has been established. This initial stage is devoid of clinical manifestations, but bacilluria can be proved. In this stage the disease cannot be demonstrated radiographically. Under modern chemotherapy cicatricial stenosis of the neck of the calyces, hydrocavities, and ureteral strictures may occur. There is, therefore, the danger of inactivation of the disease in the kidney, without an actual cure being achieved. Medical treatment should, therefore, be continued for a year or two.

Dangers in Cardiac Therapy.—K. Beyrer (*Med. Klin.* 54:487, 1959) stated that the danger of glycoside intoxication exists when an absolute overdose is given, when marked diuresis has led to hyponatremia and hypopotassemia, and when an injudicious combination, such as strophanthin with digitoxin, is used. Since the physician must always be on the lookout for signs of poisoning, routine treatment is not possible. It is often thought that severe insufficiency of the right heart requires large doses of digitalis for recompensation, but in most patients the contrary holds true. The most appropriate digitalis effect for the individual patient is often close to the toxic level.

In many patients, only a thorough examination will show whether genuine intoxication has occurred in the course of glucoside treatment or whether it has only been mimicked by such other disorders as electrolyte shifts, infections, and vascular complications. Added diuretics often cause electrolyte and fluid shifts which lead to symptoms resembling those of an overdose of digitalis and signs of intoxication due to reduction of the cardiac digitalis tolerance. Such conditions can be relieved by acidification and administration of potassium.

Often it is not easy to answer the question of whether a disturbance of cardiac rhythm is due to too much or too little digitalis. Sinus bradycardia is indicative of intoxication only if the rate falls below 55 beats per minute. When arrhythmias occur only during digital treatment the medication should be suspended for a few days. If they were present before, treatment may be continued. Digitalis intoxication frequently begins with gastrointestinal symptoms associated with ventricular extrasystoles. At this stage the medication should be discontinued for three or four days. If the drug therapy is continued, double and triple rhythm often follow and frequent polytype extrasystoles become imminent. These are often the precursors of fatal ventricular flutter and fibrillation. Further digitalis medication at this stage may threaten life. Double rhythm without digitalis is an ominous sign and requires digitalis. Massive diuresis in digitalis intoxication after the use of mercurial diuretics may elicit the dreaded ventricular tachycardia.

Treatment of glycoside intoxication is begun by withdrawing the preparation. Intramuscular injections of chlorpromazine, administration of caffeine, cocarboxylase, and atropine, and restoring electrolyte and pH balance have proved valuable. Digitalis is contraindicated in chronic nephritis, chronic obstruction of the urinary passages with renal impairment, and diabetic polyuria. Damage from diuretic treatment is to be expected when it is given in cardiac edema but is not, or is insufficiently or too late, combined with digitalis. This leads to hyponatremia and hypopotassemia. In insufficiency of the right heart the diuretics can be given after digitalization only as an adjuvant but never primarily and continuously. Since, in the presence of hepatic damage, especially cirrhosis, there is a great tendency towards hypopotassemia, particular caution is required in their administration.

INDIA

C-Reactive Protein and Ischemic Heart Disease.—Pinto and Gajjar (*Journal of J. J. Group of Hospitals and Grant Medical College* 6:249 [Oct.] 1959) recorded their experience with the use of C-reactive protein (CRP) tests as a diagnostic aid in 40 patients with ischemic heart disease. The CRP level was raised in 20 of 22 patients with transmural infarction, and the serum glutamic oxalacetic transaminase (SGO-T) level was also raised in 19. The electrocardiographic findings were positive in all, were the most useful in establishing the diagnosis, were the first to be positive, and remained so for at least two months. The SGO-T estimation is more specific for diagnosing myocardial infarction as its liberation depends directly on necrotic changes, while the CRP level would be raised in such other conditions as acute inflammation.

Thus for this type of patient CRP was found to be inferior to SGO-T, but it was superior to such other tests as determination of the sedimentation rate and the leukocyte count. These tests depend on many factors while the CRP test depends on only one, the presence of CRP in the serum. CRP tests showed positive results earlier than changes in the sedimentation rate and also showed positive results in patients who had myocardial infarction with shock when the sedimentation rate was normal. The CRP level was markedly increased in all the five patients with nontransmural infarction when the sedimentation rate and leukocyte count were not increased and the SGO-T level was normal in four of the five. The changes in CRP, when it was present, were seen even earlier than those in the ECG. In this type of patient estimation of the CRP level is therefore of special value and proved better than SGO-T tests.

In the five patients with angina CRP and SGO-T levels were unaltered. The CRP test also showed negative results in patients with impending infarction. This would serve to differentiate patients with impending infarction with negative results for the CRP test from those with nontransmural infarction but with positive results for the CRP test and may aid in planning treatment without anticoagulants in the latter group. It should be included in the treatment as an absolute indication for those in the former group. In patients with masked infarction the CRP level was raised in four of five, which confirmed the results of SGO-T estimations which were raised in all. The extent of the increased CRP level and the duration of this increase helped to determine the size of the infarct and therefore the prognosis. An early rise persisting for a long time would indicate a large infarct and therefore an unfavorable prognosis.

Bundle-Branch Block.—N. R. Mehta studied a series of 45 patients with bundle-branch block to determine the relative frequency of right and left bundle-branch block and the difference, if any, in the prognosis of the two (*J. Indian M. A.* 34:130 [Feb. 16] 1960). The diagnosis was based on the unipolar chest leads. Of the 45 patients 24 had right and 21 had left bundle-branch block. Hypertension, myocardial infarction, and coronary insufficiency were the causative factors in 58.3% of the patients with right and 85.5% of those with left bundle-branch block. This explains the occurrence of left bundle-branch block in the older age group. Congenital heart disease and rheumatic heart diseases were etiological factors in patients under 40 years of age. All but three patients had evidence of serious organic heart disease. Of the 45 patients 10 died (6 of myocardial infarction and 1 each of coronary insufficiency, atrial septal defect, rheumatic mitral valvular disease, and syphilitic aortic regurgitation). The author concluded that the prognosis was governed by the underlying cause rather than by the side on which the bundle-branch block occurred.

Maxillary Sinusitis.—J. T. Shah (*Indian J. Otolaryng.* 11:194 [Dec.] 1959) reported good results with the use of a polyethylene tube in the treatment of chronic maxillary sinusitis. This method was used to avoid the discomfort of repeated punctures and also as an alternative to such radical procedures as the Caldwell-Luc operation. While the patient was under local anesthesia the tube was introduced through a straight cannula of slightly larger bore after antrum puncture. The cannula was removed after introduction of the tube which was left inside with its distal end in the vestibulum nasi. Further lavage was accomplished by the use of a syringe and needle introduced into the antrum through the tube. This was done on alternate days until clear fluid was returned. Another lavage was given after an interval of seven days and, if clear fluid was returned, the polyethylene tube was removed. Antibiotics were used locally, and hyaluronidase was also used in severe cases.

When secretions were thick and viscid Alevaire was also used with good results. A total of 15 patients were so treated. In one patient the indwelling tube was used on both sides. The number of washings required varied from 3 to 14, and the tube was kept in place for from 14 to 60 days with no untoward results. There were relapses in only two patients. Complications were minimal. In one patient the tube slipped out of place and had to be reinserted. Another patient developed tenderness and slight swelling at the tip of the nose due to irritation caused by the end of the tube but this subsided in a few days. The results on the whole were gratifying.

Hydrochlorothiazide for Hypertension.—N. J. Shah and co-workers (*Journal of the J. J. Group of Hospitals and Grant Medical College* 4:278 [Oct.] 1959) found hydrochlorothiazide a good adjunct to other antihypertensive drugs in certain patients with high blood pressure. This drug was used, along with rauwolfia or rauwolfia and mecamylamine, in a clinical trial on 16 patients who had benign diastolic hypertension. These patients had grade 1 and grade 2 hypertension. Their ages varied from 35 to 60 years. After a preliminary period of four days of bed rest rauwolfia preparations were administered for one week. Seven patients responded well to rauwolfia alone; in the remaining nine treatment was then supplemented with hydrochlorothiazide in doses of 25 mg. two or three times daily for two weeks. Hydrochlorothiazide was then withdrawn, and rauwolfia alone was used for another week to assess the antihypertensive action of the former.

Five patients showed a good response to this combination. Two who were less than 50 years of age showed a persistent diastolic pressure of 110 mm. Hg and grade 2 changes in their eyegrounds. A ganglion-blocking agent was administered with satisfactory results. The two remaining patients, who were over 50 years of age, had grade 1 hypertension and did not show any response to combined treatment with rauwolfia and hydrochlorothiazide. No toxic reactions due to hydrochlorothiazide were noticed except in one patient who complained of muscular weakness. There was no indication of increased diuresis as revealed by a daily urine output and weight chart. The authors recommended a liberal intake of fruit juice, or some other potassium supplement, when this drug is used, in order to avoid side-effects from potassium loss.

NIGERIA

Amino Acids and Kwashiorkor.—It has long been known that a protein deficiency occurs in patients with kwashiorkor, but there is little information on the free amino acids in the plasma and urine of patients with this condition. Edozien and co-workers examined specimens of these by paper chromatography (*Lancet* 1:615, 1960). In Nigeria 50 children aged 1 to 4 years who had kwashiorkor were given glucose-water with added potassium chloride until the day after hospitalization, when fasting blood and urine specimens were collected. Similar specimens were obtained from 25 healthy Nigerian children in the same area. The blood plasma was deproteinized, desalted, and subjected to paper chromatography with use of the solvent systems butanol-pyridine-water solution or butanol-acetic acid-water solution, followed by phenol-water-ammonia solution.

The mean values for the fasting plasma amino acid nitrogen level in the children with kwashiorkor were 2.5 and 2.1 mg. per 100 ml., with use of the Folin and ninhydrin methods respectively. The values for the normal controls were 5.2 mg. and 4.3 mg. per 100 ml. respectively. In patients with kwashiorkor, therefore, the plasma level of amino acid nitrogen was about 45% of normal. In the children with kwashiorkor there was an amino-aciduria of renal origin and increased excretion of ethanolamine and β-aminoisobutyric acid. The evidence suggested that the ethanolaminuria was due to a metabolic block in the utilization of ethanolamine. The excess of β-aminoisobutyric acid could be derived from a similar block in its utilization or, alternatively, from desoxyribonucleic acid released by tissue breakdown and from a general increase in the rate of cell turnover. Both ethanolamine and β-aminoisobutyric acid were absent from the plasma and urine of control subjects. The plasma amino acid chromatograms of the children with kwashiorkor all showed a general decrease in the intensity of the spots stained with ninhydrin. The amino acids chiefly affected were cystine, methionine, valine, tryptophane, leucine, phenylalanine, threonine, and arginine. Some affected children given supplements of methionine showed a marked increase in all the plasma amino acids and a reduction in or disappearance of the excretion of ethanolamine. The excretion of β-aminoisobutyric acid was unaffected by the methionine.

SWEDEN

Development of Atherosclerosis.—Malmros and Wigand (*Nord. med.*, Jan. 28, 1960) reported that the serum cholesterol level of healthy persons rose on a diet of milk fat and coconut fat, whereas it fell when the only fat in the diet consisted of corn oil. When the fats of their diet were restricted to this oil, subjects with a history of myocardial infarct and a cholesterol level of over 300 mg.% showed a return of this level toward the normal. In another series of experiments, a diet containing 8% hardened coconut fat was fed to rabbits, which developed typical atheromas although their food contained no cholesterol. These observations suggested that the behavior of atherosclerosis can be largely determined by the choice of the fats in the diet.

Hospital Infections.—In a hospital in Malmö, Dr. S. Windblad (*Nord. med.*, Jan. 14, 1960) made resistance tests of the staphylococci isolated from the throats and noses of the staff and patients, with special reference to Staphylococcus aureus. Of the 524 staff members examined, 231 proved to be carriers. This gave a carrier rate of 44%. Among the 41 doctors, 23 were found to be carriers. This rate was 56%, whereas it was only 36% for the 33 students and porters, among whom 12 carriers were found. The carriers were almost equally distributed among the different hospital departments, with the plastic surgery department heading the list with a rate of 67.9%.

The sensitivity patterns of the staphylococci carried by the hospital staff showed more or less resistance to penicillin in 60%, to sulfonamides in 28%, to streptomycin in 34%, and tetracycline in 16%. Carriers of penicillin-resistant strains were most frequent in the staff members of the contagious, plastic surgery, and thoracic surgery departments. Inpatients examined soon after admission had strains resistant to penicillin in 42%, to sulfonadimes in 20%, to streptomycin in 26%, and to tetracycline in 11%. These rates were much increased after residence in hospital. The observation that the sensitivity patterns were identical week after week in a small group of the staff of the surgical department suggested that the staphylococcus strain in each carrier remains the same for a long time.

Drug-Induced Anemia and Kidney Disease.—Dr. L. Forsberg (*Nord. med.*, Feb. 18, 1960) described the sallow and cyanosed customers whom pharmacists serve over the counter with such drugs as acetophenetidin and acetanilid, which do not require a physician's prescription. In a series of 23 such patients many had taken acetophenetidin for several years for the relief of headache, lassitude, or depression. A daily dose of 1 to 2 Gm. was common, and in 13 instances there was a record of more than 10 years of this habit. Only two of these patients had a hemoglobin rate over 70%. In 10 it was under 50%. Reticulocytosis was demonstrable in most of these patients. In only two was there a history suggesting that the kidneys had been involved before the patients had started taking the drug. Among the four patients who died of uremia were two whose addiction to analgesics had been started by painful joints. The postmortem finding in three cases was chronic nonspecific pyelonephritis.

UNITED KINGDOM

Automation in Surgery.—Automation may soon be introduced into surgical operations to lessen the risk of infection rather than to increase the number of patients treated. Mechanical lifting and conveyer belts will replace the handling of instruments and thus reduce the number of personnel required in the operating room. Instruments will enter on a conveyer belt passing through a hatch. The first operating room of the new type will be at the Plastic and Oral Surgery Center, Odstock Hospital, Salisbury. All the instruments and appliances for the whole hospital will be sterilized in one unit and delivered automatically. Conveyer belts will also remove them for cleaning and resterilization. This is part of the answer to the increasing incidence of infection in hospitals. The contact of possible carriers with instruments and equipment will be reduced to a minimum. The new method will also reduce the chances of inadequate sterilization, as this will be done on a large scale with adequate precautions.

CORRESPONDENCE

FORCED RESEARCH

To the Editor:—The excerpt from Professor Barzun's book which appeared in The Journal, Jan. 30, page 457, suggests that the overt criticisms involved may be directed toward medical investigators as well as to their subjects of investigation, but when one analyzes the charges it becomes apparent that they cannot be leveled, with any significance, at most men in medicine. Surely the major motivations for pursuing medicine, patient-directed, academic, or investigative, cannot be "travel, secretarial help, and freedom from teaching." Nor does service in medicine combine any undue "lucre with glory." Particularly at the academic level the contrary viewpoint can be easily upheld. Are most medical studies merely a "pretense of research?" The editorial on page 456 of the same issue entitled "The Intermedium of Information" suggests otherwise. Furthermore, the latter editorial refers to the practicing physician's efforts to keep abreast to what is new in medicine. Let us keep in mind that there are not "thousands of young men . . . at work on little papers" in some limbo in medicine. The work of all but a few may be judged as little, but this work is still a compound of senior supervision (teaching) at all levels, not excluding the editorial. It is easy to understand why, in medicine, research and teaching are usually considered an integral function.

Patently, the leaders in American medicine are distinguished as teachers, investigators, and health service workers. Most of the travel of these men is an obligation; the teaching, at every level, is a privilege and a joy. It has long been obvious that lengthy pedantic lectures do not constitute teaching. Rather, informal seminars and discussions in the laboratories, at bedsides, and in the animal rooms, without regard to time and at the expense of tearful if not baleful protests from wives are the most precious times of medical learning and teaching. Indeed, academic medicine is deeply committed to the principle so elegantly presented by Sosman as "Docendo Discimus" (*New England J. Med.* 254:1105 [June 14] 1956).

Communication by some of the younger men may be forced, but Pope suggests in his "Essay on Criticism" that "true ease in writing comes from art, not chance as those move easiest who have learned to dance." The same author in his "Essay on Man" notes that "words are like leaves which most abound—much fruit of sense beneath is rarely found." Still, the ritual groaning "at the bad writing, excessive length, and prevailing insignificance of what the journals print" is no excuse for avoiding communication. Subjected to proper criticism and revision (a teaching process), each communication becomes valuable to a number of people. If we all knew what the results would be or who would be sparked by which writing, then all our efforts would be immeasurably simplified. Meanwhile, until the new golden rules are handed to us, we must carry on the work of the medical scholar, which, like the work of all scholars, is to investigate and to communicate.

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AVERAGE WEIGHT IN PERSONS OVER 65 YEARS OF AGE

To the Editor:—Master and others in their article, "Tables of Average Weight and Height of Americans Aged 65 to 94 Years," in The Journal, Feb. 13, page 658, have drawn the following conclusions. "After 65 years of age mean weight decreases progressively with advancing age in both sexes at every inch level of height. This decrease is due to loss of body substance, i. e., protein, water, fat, and calcium, which is the physiological accompaniment of aging."

In the aged there is marked reduction in physical activity which results in disuse atrophy of muscles. For comprehension of its effect on metabolism, cognizance must be taken of the following facts. Carbohydrate and protein cannot be stored dry but retain with them three or more parts of water, while fat can be stored in an almost pure state. One gram of adipose tissue gives the body 8.3 calories of reserve energy, while retention of 1 Gm. of water-soaked glycogen or protein provides only about 1 calorie. Thus 1 lb. (0.45 kg.) of adipose tissue has a value of 3,500 calories, while 1 lb. of muscle has a value of 465 calories.

The loss of 16 lb. (7.3 kg.) of muscle will result in a loss of 4 lb. (1.8 kg.) of protein (7,450 calories) and 12 lb. (5,460 ml.) of water. The loss of this large amount of water does not affect the water balance of the body. If the subject is on a diet adequate to maintain caloric equilibrium, the 4 lb. of protein will be converted into an isocaloric amount of adipose tissue, which in this instance is 2 lb. (0.9 kg.) The net loss of 14 lb. (6.4 kg.) of body weight will cause no change in the original caloric value of the body. Thus, when there is a conversion of muscle into adipose tissue, a decided weight loss occurs even though the subject is in caloric equilibrium. Parenthetically, it may be stated that early in a person's life, when a marked positive nitrogen balance is present, the process is the reverse of that which occurs in the aged; although the subject may be in caloric equilibrium, a marked increase in weight occurs. The amount and rate of loss of body weight will depend on the size of the original muscle mass and the rapidity and amount of muscle atrophy.

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NEW SYNDROMES AND THE SMALL AUTOMOBILE

To the Editor:—On four occasions within the past six months, symptoms have been encountered related to a change in the patient's driving habits. In two patients substernal and precordial pain was traced to the recent acquisition of one of the larger imported sports automobiles with a manually operated gear shift and without power-assisted steering. In two others significant and persistent pain in the left hip and left side of the back was correlated with the use of one of the new small automobiles. In all four patients physical findings were either absent or limited to mild muscle spasm or tenderness in the affected area. Roentgenograms showed no joint or bone lesions, and the electrocardiograms in the patients with chest pain showed normal findings.

A feature common to all four patients was the initial tendency for symptoms to develop a day or two after the use of the vehicle involved, so that an immediate cause-and-effect relationship was not apparent. Once the syndrome was well established, however, its relation to operation of the vehicle was obvious. At this stage, symptoms began to occur while the patient was driving the automobile or shortly thereafter and were usually relieved by abstinence from driving. Cessation of symptoms was never immediate, however, and might require as long as two or three weeks to subside, probably because, once the diagnosis was established, the patients were content to live with their discomfort.

Modern automobiles have a lowered silhouette with an acutely angled windshield, which greatly hampers entry and exit. The smaller automobiles may add the additional problem of narrower doors and often depressed floors and offset control pedals. Difficulties in operating these machines is not confined to persons 6 ft. tall; in only one instance was the patient more than 5 ft. 10 in. in height.

While the occurrence of backache will usually be readily correlated with driving in a cramped position, the enthusiast may tend to forget that he is using the muscles of the chest and shoulder girdle in a fashion to which he is not accustomed when he first acquires his new automobile. The hip and back symptoms are compatible with a bursitis or myositis resulting from the extreme rotatory motion of the trunk and abduction of the left hip, which is the technique which the average person instinctively seems to assume when faced with the problem of entering or leaving the automobile. Last, and perhaps as important in causing the hip and back symptoms, the limitation in footroom due to intrusion of the wheel well into the front compartment compels the driver and frontseat passenger to sit with the lower half of the body rotated in order to secure the maximum available space. Furthermore, once this position is assumed, there is usually no alternative position for the feet, as there may be in larger automobiles.

While it is unlikely that the individual practitioner will see many cases of "Jaguar chest" or "Corvette hip," the increasing popularity of smaller automobiles and the renaissance of the gearshift lever should be a warning to the clinician to be on the lookout for new musculoskeletal syndromes.

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LESIONS OF ASCENDING COLON

To the Editor:—In two recent articles, lesions of the ascending colon have been intimated to be cecal. By definition (Thorek: Anatomy in Surgery, Philadelphia, J. B. Lippincott Company, 1951; Turell: Diseases of Colon and Anorectum, Philadelphia, W. B. Saunders Company, 1959, vol. 1; Spalteholz: Handatlas der Anatomie des Menschen, Leipzig, Verlag von S. Hirzel, 1920, vol. 3), the cecum is that portion of the large intestine of which the distal limit is the ileocecal valve. Accordingly, that part of the colon immediately above or distal to this site is part of the ascending colon.

In the article by Waggener and others entitled "Asymptomatic Tuberculous Enteritis Simulating Carcinoma of the Cecum" in The Journal, Nov. 7, 1959, page 1337, it is stated that "roentgenographic examinations of the colon with use of the barium enema revealed a persistent filling defect of the middle of the ascending colon," and the legend beneath figure 1 reads as follows: "Roentgenographic study of colon, showing filling defect in ascending colon." The title of the article is misleading. The preoperative diagnosis was adenocarcinoma of the ascending colon. At operation, "a large, firm, irregular, and constricting lesion of the ileocecal region was found" and the "gross appearance of the lesion suggested an adenocarcinoma." Why did it "simulate a carcinoma of the cecum" instead of one of the ascending colon?

Daniels and Wood, in their article entitled "Diverticulitis of Cecum and Ascending Colon," which appeared in The Journal, Feb. 6, 1960, page 519, state that "a barium enema roentgenogram revealed several diverticula of the ascending colon, just above the ileocecal junction." The legend accompanying figure 4 (case 3) describes "outpocketing attached by a wide neck just above ileocecal junction" as a "diverticulum of the medial side of the cecum." Obviously, the statement about the roentgenogram is true and the statement in the legend about the anatomic site is not true.

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The above comment was referred to the authors of the article mentioned first, and they have submitted the following reply.

To the Editor:—The comment by Dr. Flora is justified, as the terminology used in our article is misleading. The roentgenograms appeared to reveal a defect in the ascending colon, but the barium-filled intestine proximal to the lesion was actually the dilated terminal part of the ileum. Thus the roentgenogram was not and could not have been interpreted correctly. Anatomically, the lesion was located in the cecum and terminal ileum. We elected to include the radiologist's interpretation of a filling defect in the ascending colon in the text. We also should have used this term in the title even though the lesion grossly resembled adenocarcinoma of the cecum. I am grateful to Dr. Flora for calling attention to this discrepancy.

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STERNAL TRACTION

To the Editor:—In the article in The Journal, March 12, page 1138, by Craighead and Glass, entitled "Management of Nonpenetrating Injuries of the Chest," figure 1, showing stabilization of flail chest by sternal traction, and figure 2, showing the Bigelow screws and bar, are excellent, but the Bigelow screws and bar may not always be available and other means may have to be used. In the southern Pacific Ocean, during World War II, the hospital that I was in received a man with such a severely crushed chest that it is remarkable that he reached the hospital alive. One of the surgeons simply grasped each costal cartilage with a towel clamp (Backhaus) applied through the skin and attached them to an overhead bar. The patient made a good recovery. This method of costal, or sternal, traction is almost universally available.

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W. M. I.

To the Editor:—In The Journal, March 12, page 1166, in an editorial entitled "The Last of the Hopkins Four," there was comment on the death of Dr. Howard C. Kelly and a reference to a biography under the same name. When I referred to the title page of "The Vermaform Appendix and its Diseases," written by Dr. Kelly and Dr. Hurdon and published in 1905 by W. B. Saunders Company, Philadelphia, I found that the name given to the author of this work is Howard A. Kelly. My best recollection is that his middle name was Atwood. I am at a loss to understand how such an error, typographic or otherwise, was permitted to enter The Journal, and I believe that an appropriate correction is in order.

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Apologies to the late Dr. Howard A. Kelly and thanks to his former pupil, Dr. Harvey H. Musser. It is noteworthy that Henry Ernest Sigerist, the medical historian, had two different middle initials and two different middle names other than his correct ones. In the catalog of the Library of Congress he appears as Henry Ernst Sigerist (On the History of Medicine, New York, MD Publications, Inc., 1960). On the cover of the Swedish translation of his "Einführung in die Medizin" his name appeared as Henry M. Sigerist. The author of a Dutch translation of the same book is listed as Sigerist, Henry Eduard. A translation of the book into Chinese identified him as Henry S. Sigerist. W. M. I. (wrong middle initial) sometimes is irritating.

Isn't the title of the monograph by Kelly "The Vermiform Appendix and its Diseases?"—Ed.

"MEDICAL EXAMINER"—A MISLEADING TERM

To the Editor:—As a deputy medical examiner in Nassau County, I have found the term "medical examiner" to be confusing and misleading to the general public. For example, people call our office to request medical (physical) examinations and find it difficult to comprehend our refusal to perform them. I have noticed that the term "medical examiner" is used throughout the nation. It occurred to me that the word "mortology," which connotes the study of death, would be more appropriate. Then the medical examiner's office would be known as the Department of Mortology and the medical examiner as a mortologist. Any help that can be offered on the semantics of this problem would be gratefully received.

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MEDICAL FILM REVIEWS

Contact Ulcer of the Larynx: 16 mm., color, silent, showing time 11 minutes. Prepared in 1959 by Paul Moore, Ph.D., and Hans von Leden, M.D., Chicago. Procurable on rental ($5) or purchase ($75) from Hans von Leden, M.D., 30 N. Michigan Ave., Chicago 2.

Essentially, this film consists of motion pictures of the larynx in a case of contact ulcer. The patient in question developed a contact ulcer as a result of voice trauma during investigation of laryngeal function. After the contact ulcer had developed, various stages in healing were recorded by high-speed motion pictures and presented in the film. The initial part of the film demonstrates the action of the vocal cords and arytenoid cartilages during production of sound of various pitches. The more strenuous movement made during clearing of the throat and coughing is shown, and in this part of the film some variations in the action of the arytenoid cartilages are pointed out. An ulcer at the tip of the vocal process on one cord developed during the strenuous use of the larynx occasioned by the investigations. The different stages in healing observed after complete voice rest, aphonic whisper, and gentle talking are represented. The photography is excellent, clearly demonstrating the motion of the vocal cords. Some of the finer variations in the movement of the arytenoid cartilages, described in the titles, are not easily recognizable. The film is useful as a demonstration of movements of the vocal cords and of the type of trauma that might produce a contact ulcer. It is recommended for students of speech and laryngology.

It's Wonderful Being A Girl: 16 mm., color, sound, showing time 19 minutes. Produced in 1959 by Audio Productions Inc., for Personal Products Corporation, Milltown, N. J. Procurable on loan or purchase ($77) from Audio Productions, Inc., 630 9th Ave., New York.

The purpose of this film is to encourage a healthful knowledge of the menstrual process and positive attitudes for girls who are just beginning to menstruate. On her 14th birthday, Linda Brown decides that it's wonderful to be a girl growing up. It's wonderful to have parties and dates, make new friendships, learn new skills, and develop your talents. It's wonderful to know about yourself, recognize your bodily changes, and understand what menstruation is and how to live with it happily. This film story covers a year of Linda's life and shows how she arrives at these happy conclusions. She learns from her mother what to expect when menstruation occurs. She begins to scorn the old wives' tales she has heard and the superstitious attitudes she has seen. When she begins to menstruate, she finds that it need not hamper her in successfully meeting the challenges of everyday life. At school a teacher's thorough explanation, brought to life in colored, animated drawings, provides Linda with the important facts about how she became the girl she is: the origin of life in a single cell, the changing physical characteristics of a girl in her early teens, and the purpose and psychological processes of menstruation. Discussions in the class reveal that a girl's menstrual periods need not limit her activities. Through her own social experiences with girls and boys in her hobby club, at the school picnic, at parties and in other activities, Linda discovers that regular meals, sleep, and exercise help her to take menstruation in stride with the other normal problems and pleasures of growing up. This film is to be commended for its emphasis on the fact that menstruation is a perfectly normal process in the life of girls. It helps to create proper attitudes for girls who may have some problems in adjusting to menstruation, particularly in the beginning. The story is well developed and the film is effective because it closely approximates life situations for girls in this age group. Good mother-daughter and teacher-student relationships are demonstrated. It is unfortunate that the sponsor included a brief scene about their product. This may restrict use of the film in some schools. This picture is recommended for the audiences for which it was intended, namely, girls in elementary and junior high school. It would also be of interest to parents, teachers, and those in teacher training.

Branchial Cleft Cysts and Sinuses: Their Embryologic Development and Surgical Management: 16 mm., color, sound, showing time 13 minutes. Prepared in 1959 by William H. ReMine, M.D., Rochester, Minn. Procurable on rental ($3) from Motion Picture Library, American College of Surgeons, 40 E. Erie St., Chicago 11.

The film begins with a review of the embryology of the branchial grooves, clefts, and pouches. Noteworthy emphasis is placed on the importance of the second cleft, particularly its relationship to the anomalies which occur in this region. The narrator, however, correctly stresses the point that its importance is still a moot question. Preliminary presentation is then reviewed and amplified with colored illustrations which considerably clarify much of the previously read material. A clearer visual concept of the subject matter might be obtained by the viewer if these illustrations were used earlier in presentation. Two surgical cases are then presented, the first dealing with branchial cleft cysts and the second with a branchial sinus. The cysts were readily removed through a small transverse incision placed directly over the mass, by both sharp and blunt dissection. The dissection was neat and clean, with exposure of the internal jugular vein and common carotid artery, and the vagus nerve was clearly depicted. The branchial sinus was removed by a stepladder procedure or multiple incision technique. This was dissected amply to its origin at the pharynx. The photography is good and the narration well paced and comprehensible. This film is to be recommended to anyone who is interested in the surgery and embryology of branchial pathology.

MEDICAL LITERATURE ABSTRACTS

INTERNAL MEDICINE

Systemic Lupus Erythematosus After "Idiopathic" Thrombocytopenic Purpura: A Review: A Study of Systemic Lupus Erythematosus Occurring After 78 Splenectomies for "Idiopathic" Thrombocytopenic Purpura, with a Review of the Pertinent Literature. Y. Rabinowitz and W. Dameshek. Ann. Int. Med. 52:1-28 (Jan.) 1960 [Lancaster, Pa.].

The authors had previously emphasized the close relationship between idiopathic thrombocytopenic purpura (I. T. P.) and systemic lupus erythematosus (S. L. E.) and had suggested that I. T. P. is often a prodrome of S. L. E. Although there had been reports on the incidence of I. T. P. in S. L. E., there were none on the incidence of S. L. E. in I. T. P. The authors approached this problem through the reevaluation of their patients with I. T. P. who had been subjected to splenectomy, which ruled out most of the acute cases of I. T. P. Until 1955 they had generally performed splenectomy on all patients in whom thrombocytopenia persisted for 4 months or more, these cases being considered chronic.

Letters of recall were sent to all patients whose spleens had been removed because of I. T. P.; those who responded were reexamined, their records were reviewed, and various hematological studies were made. Among 51 patients with I. T. P. who had undergone splenectomy after 1949, there were 8 with definite, 2 with probable, and 6 with possible S. L. E. Although follow-up was limited in 27 patients with I. T. P. on whom splenectomy had been performed before 1949, this group included 4 patients with definite and 2 with possible S. L. E. (More complete follow-up would probably have revealed a higher incidence.) In 2 other definite cases splenectomy had been performed elsewhere. Thus, among a total of 78 patients there were 14 with definite, 2 with probable, and 8 with possible S. L. E. The authors suggest that the presence of discoid lupus and of I. T. P. is characteristic of definite S. L. E. in that it became evident from their studies that discoid lupus is simply a dermatological manifestation of the generalized vasculitis of the disease, and that it may either precede or follow the onset of I. T. P. or the other manifestations of S. L. E. Failure of response to splenectomy or relapse of thrombocytopenia appeared to be of the same frequency in patients in whom S. L. E. was detected after splenectomy for I. T. P. as in I. T. P. in general.

Exacerbation of S. L. E. occurred in 2 of the 14 definite cases after splenectomy. The development of S. L. E. in cases of I. T. P. treated with prednisone and without splenectomy has not been studied because sufficient time has not yet elapsed. It is possible that this drug will suppress the manifestations of S. L. E. Of the 78 patients reviewed, 69 were women; other reports likewise indicate a great predominance of female over male patients in S. L. E. as well as in I. T. P. One of the authors suggested that this predominance of women may have an etiological significance. In menstruation, blood cells and endothelium are shed each month in an environment of open blood vessels. Some of these altered tissues are perhaps absorbed into the circulation, to become antigens in an autoimmune process. The authors feel that the high incidence of S. L. E. in this series indicates the need for considering it in every patient with I. T. P.

Staphylococcal Endocarditis. P. Lisan, J. F. Uricchio, D. J. Marino, and others. Am. Heart J. 59:184-190 (Feb.) 1960 [St. Louis].

The records of the bacteriology department of Hahnemann Medical College and Hospital, Philadelphia, from 1949 to 1958 were used in this study. Charts of all patients who had 2 or more positive blood cultures for Staphylococcus pyogenes were reviewed, and the study was limited to those with definite evidence of bacterial endocarditis. There was a total of 38 such patients, 22 males and 16 females, ranging in age from 2½ to 70 years. The antecedent heart disease was rheumatic in origin in 33 of the patients, and in 5 it was congenital. Twenty-one of the patients had previously undergone cardiac surgery. The staphylococcic endocarditis developed immediately after surgery in 7 of these 21 patients, within 4 months in 11 others, and in the remaining 3 within 1 year. Fever was noted in all 38 patients and was the presenting complaint in all but 3 of them.

Penicillin, administered by intramuscular or intravenous routes, was used initially in most of the patients. The dosages ranged from 100,000 to 50 million units per day. When the organism was identified (disk method) and the in vitro sensitivity

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The place of publication of the periodical appears in brackets preceding each abstract.

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determined, appropriate changes were made in therapy. In 5 patients wide-spectrum antibiotics (chlortetracycline, oxytetracycline, or chloramphenicol [Chloromycetin]) were given because the organisms were sensitive only to these drugs. Chlortetracycline, oxytetracycline, and chloramphenicol used singly accounted for 3 recoveries. The remainder of the patients who were cured received combinations of several antibiotics. A choice of antibiotics, however, cannot be reliably made in in vitro sensitivity studies alone. There is little correlation between the disk sensitivity method and the success of the more sensitive antibiotics in curing staphylococcic endocarditis. As a matter of fact, penicillin was found to be ineffective, in vitro, in most cases of staphylococcic endocarditis; yet it produced, alone or in combination, the greatest number of recoveries when used in large doses.

Deaths from staphylococcic endocarditis have greatly increased in recent years. Furthermore, staphylococci are the cause of bacterial endocarditis more often now than are streptococci of the viridans group. Operative procedures within the heart and its major vessels are an important factor in predisposing patients to a staphylococcic infection of the endocardium. This is evidenced by the fact that 2 of every 3 patients with staphylococcic endocarditis had had previous cardiac surgery. On the other hand, the over-all incidence of staphylococcic endocarditis in patients undergoing cardiac surgery is extremely small, only 21 instances occurring among 3,600 heart operations in a 10-year period.

A Study of 500 Consecutive Admissions to a Tuberculosis Hospital. C. A. Wicks. Am. Rev. Resp. Dis. 81:161-172 (Feb.) 1960 [New York].

The author reports on 281 male and 216 female patients who were admitted to the Toronto Hospital for Tuberculosis in Weston, Ont., Canada, between January and August, 1957. Of these 497 consecutive patients, 405 (81.5%) had tuberculosis of the respiratory system as the most important problem, 66 (13.3%) had other forms of tuberculosis predominantly, and 26 (5.2%) had nontuberculous disease only. A review of age, sex, familial descent, and country of birth confirmed that this group of patients was reasonably representative of patients admitted to tuberculosis hospitals in recent years. Of the 497 patients, 350 were admitted for the first time, 84 were readmitted for treatment, 39 were transferred from another hospital, and 24 were readmitted for review of the status of their disease. An attempt was made to correlate such factors as extent of tuberculosis, presence of cavities, and drug resistance with therapeutic progress in the hospital during 18 months after entry for patients who were first admissions and readmissions with active pulmonary tuberculosis.

Among this group, the therapeutic progress was shown to be least satisfactory for those who were readmitted to the hospital, had far-advanced pulmonary tuberculosis, had definite cavitation, had tubercle bacilli in the sputum and tubercle bacilli resistant to streptomycin, aminosalicylic acid (PAS), or isoniazid, and were not suitable for pulmonary resection. These findings seem to suggest the lesson that, in the management of tuberculosis, there is no substitute for early diagnosis followed by prompt, carefully supervised, and adequate treatment accepted by a cooperative patient.

Thyroiditis: Classification, Etiology, and Clinical Features Observed in 49 Cases. E. H. Yount. South. M. J. 53:129-133 (Feb.) 1960 [Birmingham, Ala.].

This report is concerned with the clinical features of thyroiditis as observed in 49 patients seen in the North Carolina Baptist Hospital, Winston-Salem, during the 10-year period from 1948 to 1958. This group included only one patient with acute suppurative thyroiditis, a condition which has been known to occur after dental infections or extractions. The suppurative process tends to localize within a nodular goiter, but if the thyroid is normal, the process will be diffuse. When aspiration permits identification of the organism and determination of its drug sensitivity, the administration of antibiotics is most effective. Surgical incision and drainage are indicated when there is abscess formation.

In *nonsuppurative subacute thyroiditis*, which has been described also under such terms as acute noninfectious thyroiditis, acute diffuse thyroiditis, and subacute thyroiditis, the pathological findings have been identified as granulomatous thyroiditis, pseudotuberculous thyroiditis, giant-cell thyroiditis, and struma fibrosa. Of the 49 cases reviewed by the author, 25 were of the subacute type of thyroiditis. This disorder is usually self-limited. Only 3 patients were subjected to operation. Palpation revealed diffuse enlargement of the thyroid and an abnormally firm or hard consistency. Evaluation of therapeutic measures was difficult because of the tendency to spontaneous healing and the variable duration of the disease. The use of antibiotics and antithyroid drugs, such as prophylthiouracil, has been of little or no benefit. Administration of adrenal corticosteroids almost invariably suppresses the inflammation and the other symptoms, but withdrawal of corticosteroids may be followed by recurrence.

Of the 2 forms of chronic thyroiditis, Hashimoto's struma and Riedel's struma, the first is much more frequent. Although Hashimoto's struma was observed in 23 of the 49 patients, not a single case of Riedel's struma, also known as ligneous thyroiditis or invasive fibrous thyroiditis, was observed during the 10-year period. Hashimoto's variety is known also as struma lymphomatosa or lymphocytic thyroiditis. With one exception, all 23 patients were women. The preponderance of women patients has been attributed to the increased need for iodine during puberty, pregnancy, and the menopause. The etiological theory currently in favor is that of autoimmunity. The suggestion has been made that Hashimoto's disease is produced when thyroglobulin is released from the thyroid and initiates an autoimmunization process. Such a release of thyroglobulin could possibly result from damage to the gland, and thyrotoxicosis or subacute thyroiditis has been suspected as the precipitating event, but none of the 23 patients gave a history suggestive of preexisting thyrotoxicosis or subacute thyroiditis. Final acceptance of the autoimmunity concept will depend on the results of further studies.

In the author's experience, Hashimoto's chronic thyroiditis produces no systemic manifestations. More than 50% of the patients complained primarily of discomfort on swallowing and of a choking sensation. The thyroid was known to have been enlarged for from 2 weeks to 30 years. Nodularity, in the vast majority of cases, was probably due to distortion of the lobulations of the gland. In early cases of Hashimoto's chronic thyroiditis, the enlargement will regress if full doses of desiccated thyroid are administered. Thyroidectomy is indicated for Hashimoto's disease when the patient desires relief from symptoms of pressure, or from a cosmetically unacceptable goiter, or when there is any suspicion of a neoplasm. Operation was performed on each of the 23 patients in this group. None of these patients has had a recurrence.

Malignant Reticulosis with Clinical Characteristics of Periodic Fever: New Case. P. Perrin, G. Dauphin, J. P. Kerneis, G. Nicolas, and P. Litoux. Presse méd. 68:140-142 (Jan. 27) 1960 (In French) [Paris].

The authors report on a case of malignant reticulosis with typical periodic fever, which they believe is the 9th case in the medical literature since Mollaret defined and identified the disease in 1950. This condition, always fatal, is characterized by the thermic curve which shows waves of fever of 4 or 5 days' duration, separated by 14-day apyretic periods. The patient, a 47-year-old man, first noticed a cervical adenopathy on the right, a mobile and painless nodule. Findings from a biopsy of this nodule suggested Hodgkin's disease, and the patient received 8 radiotherapeutic applications totaling 2,000 r. During the next year the patient was kept under observation, without any treatment. The febrile phases took place regularly, and the general condition deteriorated steadily, although the patient had a good appetite. Fifteen months after the onset of the disease the results of the physical examination were still negative, except for a painless hepatosplenomegaly. In the course of a periodic febrile phase the patient was given 20 mg. of prednisone; the next day the fever had subsided. After another 24 hours prednisone was withdrawn, and the fever recurred within a few hours. Therapy with cortisone derivatives was resumed and failed to bring any favorable results. The treatment had to be interrupted because of the side-effects, and the patient died on the 11th day of the febrile period.

Malignant reticulosis with periodic fever presents with a characteristic clinical picture and deserves to be considered as a nosological entity in spite of the small number of cases reported in the literature. The diagnosis is essentially clinical. The possibility of malignant reticulosis should be considered whenever a patient has a fever which lasts for 4 or 5 days and recurs regularly every 2 weeks. The authors believe that cortisone should be administered because of its effects on the fever and the general condition, although the ultimate results have always been disappointing.

Yellow Spinal Fluid: Diagnostic Significance of Cerebrospinal Fluid in Jaundiced Patients. D. G. Rosenberg and J. T. Galambos. Am. J. Digest. Dis. 5:32-48 (Jan.) 1960 [New York].

Bilirubin levels, color, protein levels, cell counts, and glucose levels of the cerebrospinal fluid (CSF) were studied in 62 consecutively admitted, unselected adult patients with jaundice. Viral hepatitis was present in 20 patients; leptospirosis, in 3; intrahepatic cholestasis, in 2; cirrhosis, in 14; Hodgkin's disease, in 3; benign obstructive lesions, in 2; malignant obstructive lesions, in 9; and anemia and jaundice of unknown cause, in 9. Both direct and indirect bilirubin was present in the spinal fluid. Yellowish CSF with increased CSF bilirubin value was present in some instances in each group. The yellow color of the CSF was not directly related to elevation of the CSF bilirubin level, nor was the height of the CSF bilirubin level related to the duration of jaundice, but it was related to the serum bilirubin levels in patients with viral hepatitis and with chronic intrahepatic disease. This correlation could not be demonstrated in patients with extrahepatic obstruction. The mean of the CSF and serum bilirubin ratios was not significantly different in the groups of patients with viral hepatitis, chronic intrahepatic disease, and extrahepatic obstruction.

The presence of yellowish spinal fluid with increased CSF bilirubin value cannot be used for the differential diagnosis of jaundice; however, if pleocytosis is also present, a diagnosis of leptosirosis in a patient with jaundice is very probable. The CSF protein level was 40 mg. per 100 cc. or above in 5 patients with viral hepatitis. Polymorphonuclear leukocytes were present in the spinal fluid in 4 patients with viral hepatitis, but no pleocytosis was noted. Elevation of the CSF protein level was associated with hepatic coma or delirium tremens in patients with cirrhosis. No significant correlation between the CSF bilirubin (direct) level and the CSF protein level was observed in this series.

Augmented Histamine Test, Ewald Test Meal, and Diagnex Test: Comparison of Results. I. N. Marks and H. Shay. Am. J. Digest. Dis. 5:1-23 (Jan.) 1960 [New York].

The results of the augmented histamine test, the Ewald test meal, and the azuresin (Diagnex Blue) tubeless test were compared in a series of 130 patients. Duodenal ulcer was present in 43 patients; gastric ulcer, in 26; and atrophic gastritis, gastric cancer, pernicious anemia, and other disorders in the remainder. The 3 procedures were carried out in 74 patients, and 2 of the 3 procedures in 56 others. There was a significant quantitative relationship in the results of the 3 tests. It was also shown that no single test could be used to predict the results of the other tests. The Ewald test meal was as useful as the augmented histamine test in making a diagnosis of duodenal ulcer. The augmented histamine test, however, was more reliable for establishing the presence of achlorhydria. This test was free of any serious side-effects and provided a reliable index of the parietal-cell mass. The augmented histamine test can, therefore, be used as a guide to determine the nature and extent of surgery required for reduction of acid secretion in patients with peptic ulcer. The azuresin test is a convenient procedure for mass screening of patients susceptible to gastric cancer, but is of limited value in excluding a diagnosis of pernicious anemia or duodenal ulcer.

Systemic Diffuse Sclerosis with Dominant Renal Manifestations: Contribution to the Study of the Sclerodermic Kidney. P. Michon, G. Rauber, A. Larcan, J. Beurey, and F. Streiff. Presse méd. 68:133-136 (Jan. 27) 1960 (In French) [Paris].

The authors report on a case of systemic diffuse sclerosis with specific renal manifestations and visceral lesions disseminated throughout several organs. These renal manifestations correspond to specific anatomic lesions and carry an unfavorable prognosis, being shortly followed by death. The vascular lesions associated with the renal manifestations explain the gravity of the disease.

The patient, a 34-year-old man, was seen by the authors because of severe azotemia which had developed in the course of scleroderma of 9 years' duration. The first symptoms noticed were articular pains. A year later vasomotor disturbances in the extremities occurred, resembling the clinical picture of Raynaud's syndrome. Five years after the onset of the disease the patient presented sclerodactylia, cyanosis of the extremities, thickening of the facial skin, and marked dysphagia. Corticotherapy was instituted. In another 3 years the disease had progressed, and the patient had a typical appearance, with a rigid face and shining, varicosed teguments. His speech was slow, and eating was difficult. The thorax and abdomen were striped. Subcutaneous emphysema, marked hepatomegaly, galloping cardiac rhythm, and ventricular hypertrophy were other features. The patient was hospitalized and given treatment aimed at hydroelectrolytic balance and cardiac strengthening, but he died 10 days later, shortly after an extensive hematemesis.

Autopsy confirmed the existence of a generalized visceral involvement, with mixed and diffuse renal lesions, glomerular, tubular, and interstitial. Vascular changes were the dominant feature, being the determining factor of the cortical infarction. The renal lesions may have been aggravated by the hormonal treatment, although their onset had preceded any form of therapy. The authors stress the importance of the vascular involvement as an etiological factor in systemic diffuse sclerosis.

Differential Diagnosis of Jaundice. R. A. Cruz, G. L. Parga, and H. A. Rojas. Rev. méd. Chile 87:952-961 (Dec.) 1959 (In Spanish) [Santiago].

Two groups of patients with hepatic disease were observed, and the methods of differential diagnosis used were evaluated. Four categories of clinical diagnosis were established as a basis for evaluation, namely, certain, probable, doubtful, and suspended diagnosis. The 1st group observed was composed of 620 patients with hepatitis. In 87% of these patients the initial symptoms were anorexia, nausea, a sensation of epigastric fulness, and pain in the right upper abdominal quadrant. Generalized body pain, especially articular pain, was an important diagnostic sign, for the hepatitis virus tends to become localized in the muscles and joints. When this type of pain was associated with jaundice, the diagnosis of hepatitis was considered certain. Age was another element, since jaundice in persons under 30 years of age usually means hepatitis. Fever and chills were signs of biliary lithiasis; an insidious progressive course was found when cancer obstructed the bile flow and caused gallbladder distention. Palpation of an enlarged spleen suggested cirrhosis, sometimes hepatitis, but rarely obstruction. Determinations of blood phosphatase activity and of flocculation reactions were the laboratory tests used to supplement clinical observation when no clinical diagnosis was established. Phosphatase values tend to be elevated (above 10 Bodansky units), and flocculation reactions tend to be negative in obstructive jaundice, while phosphatase values below 10 Bodansky units, together with positive flocculation reactions, suggest hepatocellular jaundice.

The diagnostic criteria established in the 1st group were tested on a 2nd series of 100 patients with jaundice. The clinical diagnoses established in this series were certain in 80 cases, with confirmation in 76; probable in 8 (confirmed in 2); doubtful in 10 (confirmed in 4); and suspended in 2. The authors estimate that these purely clinical diagnoses were valid in 82% of the cases. A combination of clinical and laboratory findings brought the diagnostic validity up to 100%.

Porphyria in Denmark: Review and Preliminary Report. T. K. With. Ugesk. laeger 122:63-78 (Jan. 21) 1960 (In Danish) [Copenhagen].

Porphyria cutanea tarda usually manifests itself in middle age and most often in men. The congenital form generally begins in early childhood, and the sex apportionment is about equal. The dominating symptom is sensitivity to light. In some cases there is marked progression of the disease; in other cases it "burns out" after a number of years. In addition to chemical, mainly medicamental, provocation of manifest symptoms in patients with latent porphyria, irradiation, infections, and normal biological stress, such as pregnancy, can be provoking factors. The heredity factor in congenital porphyria is thought to be recessive, but in hepatic porphyria it is dominant and necessitates examination of the family history of patients with acute porphyria. About one-half of these patients' children and siblings, and at least one of their parents, are bearers of the dominant porphyria germ and should be protected from such provoking factors as alcohol and barbiturates. If latent porphyria is suspected, quantitative examination of the urine of relatives for porphobilinogen by the chromatographic method and a screen test of the feces for porphyrin will clarify the situation. Clinically, porphyria should be borne in mind in vague abdominal cases, in eruptions of a hydroa aestivale type, in acute progressive paresis of vague etiology, in vague psychic disturbances, and especially in anomalies of pigmentation and hair growth. In observation for acute porphyria, chromatographic determination of porphobilinogen is necessary. Qualitative determination, together with positive screen tests for porphyrin in urine or feces, suffices to establish manifest porphyria.

Latent porphyria is far more frequent than the manifest form, and symptoms can be induced in bearers of the germ by certain provocative factors, the most important of which now seem to be barbiturates, sulfonmethane (Sulfonal), and sulfonethylmethane (Trional). Porphyria is best met by recognizing the condition in the latent stage and avoiding the provocative factors. The prognosis for length of life in congenital porphyria is good, but attacks of acute porphyria threaten life. The special precautionary measure in a porphyria attack without paresis is avoidance of barbiturates. If paresis sets in, the treatment corresponds to that of poliomyelitis with threatened respiratory paralysis. No therapy known today is 100% effective in attacks of acute porphyria. ACTH has given excellent results in some cases. Chelation therapy and bemegride (Megimide) therapy are the only forms of treatment for the acute porphyria attack which are not purely symptomatic in effect.

An Investigation into the Incidence of Onchocerciasis in a Community Exposed to Infection. C. Boroda. East African M. J. 36:610-612 (Nov.) 1959 [Nairobi, Kenya].

The author examined 298 persons in Kilembe, Uganda, who had been exposed to the risk of bites from vectors of the Simulium genus, so as to determine if any had developed onchocerciasis in the transmission of infection with the filarial worm, Onchocerca volvulus. The persons examined were European and Asian workers and their families who had been in Kilembe for at least 2 years. The tests carried out were a differential white blood cell count and the Mazzoti test, consisting of the oral administration of a provocative dose of diethylcarbamazine citrate (Hetrazan). The latter drug was administered in 50-mg. tablets 4 times daily for 2 days to adults and in a reduced amount to children. There was no instance of positive allergic reaction to diethylcarbamazine, and no symptoms of onchocerciasis were observed. However, 9 children had an eosinophil count of more than 10%, which is generally accepted as a significant level; it proved that these patients had intestinal worm infestations. Repeated negative results were obtained in 125 persons of the same group a year after the original examination. This study suggests that either some factor prevents the development of the disease despite repeated bites from infected flies, or the incubation period of onchocerciasis may be very long.

Concerning Sarcoidosis. O. Refvem. Tidsskr. norske laegefor. 79:1435-1438 (Dec. 15) 1959 (In Norwegian) [Oslo].

Sarcoid tissue, or sarcoid granuloma, is a neutral designation for a morphologically special form of tuberculoid granuloma. Distinction is made between sarcoidosis, or genuine sarcoid, and numerous forms of symptomatic sarcoid. It is the clinician's task by evaluation of clinical and roentgenologic findings, possibly the Kveim test, and by continued observation to decide whether the patient has sarcoidosis. Emphasis is laid on the clinical symptoms. There is no pathognomonic sign. Early stages or recent manifestations show a marked tendency to spontaneous remission. Cases accompanied by erythema nodosum are thought to have a good prognosis. A not inconsiderable number of cases will persist or progress. The development must be followed by regular control (at least 3 or 4 times in the first year).

Pulmonary sarcoidosis is the form most discussed as to treatment for the prevention of development of diffuse fibrosis with emphysema, bronchiectasis, and cor pulmonale. Infiltrations in the lung parenchyma, remaining for a long time or increasing, are indications of the need for treatment, and the corticosteroids are at present the best means available. Cortisone has been found on long-term treatment to cause numerous side-effects, especially edema and development of features of adrenal cortical hyperfunction (Cushing's syndrome). Prednisolone has not caused notable side-effects with the exception of an increase in nervous phenomena in an occasional case, together with increase in weight. The danger of development of ulcer and consequent bleeding is as great with prednisolone as with cortisone. The immediate effect of prednisolone on lung infiltrations in the main has been good, and in part excellent. The treatment is carried out with careful control, and the smallest effective dose is administered in every case. Improvement can often be maintained with small doses. Duration of the treatment has been from about 9 months to 2 years.

Q Fever in the R. A. F. in Great Britain in 1958. W. W. Holland, K. E. K. Rowson, C. E. D. Taylor, and others. Brit. M. J. 1:387-390 (Feb. 6) 1960 [London].

The authors report on 2 localized outbreaks of Q fever among Royal Air Force personnel, one at a large costal command station in Cornwall and the other in a small officers' training unit in the Isle of Man, in March and April, 1958. No relation between these 2 outbreaks could be found. In the outbreak in Cornwall, 4 sick-quarters attendants and 1 visitor were probably infected from a patient 14 to 16 days after contact with the latter. No other case or any source of Q fever was found at this station. In the 2nd outbreak, half of one squadron of 45 officer cadets had Q fever. Serologic findings agreed closely with history of the illness. Nine of 34 members of the permanent staff at this station also had a raised titer of complement-fixing antibodies to Rickettsia burnetii (Coxiella burnetii). All personnel involved were concerned in some way with a visit to a shooting range and with cleaning out a hut in which lambing may have taken place. It is postulated that this was the source of the outbreak.

To assess the prevalence of Q fever in the Royal Air Force, samples of serum obtained from 154 patients who were admitted to the sick quarters of 20 stations during the period of March and April, 1958, were tested. Ten of the stations selected were situated far from towns and in parts of Britain where sheep farming is common; the other 10 stations were chosen because of their proximity to towns, and were in areas in which sheep farming is not prevalent. Only one of the 154 patients was found to have an antibody titer to R. burnetii of 1:16. One further case of Q fever was discovered at another Royal Air Force station during this investigation. These findings confirm those of Marmion and Stoker in their previous reports on the epidemiology of Q fever in Britain, in showing that the origin of most British outbreaks of Q fever remains unexplained.

Fatal Hypoglycemia: Clinical and Pathological Study. E. Concha, L. Silva, and O. Veit. Rev. méd. Chile 87:857-863 (Nov.) 1959 (In Spanish) [Santiago].

Hypoglycemia interferes with the metabolism of respiration of nervous tissues and causes characteristic lesions of anoxia in the brain. It is frequent in patients with diabetes in the course of insulin therapy, but it can be controlled by early and adequate treatment. Adequate treatment consists of diminishing the dose of insulin to the minimal optimal dose for the particular patient and giving him an intravenous injection of 1,000 cc. of hypertonic dextrose solution.

Six cases of fatal hypoglycemic coma in patients with diabetes in the course of insulin therapy are reported. The patients were 36 to 70 years of age. They had had diabetes for several years. Five were poorly nourished. Four had had hypertension for several years. One had had a cerebral hemorrhage 24 hours before the occurrence of coma. One had tuberculous meningitis and yellow atrophy of the liver. Two had undergone an operation 2 days before the coma. Two had had previous attacks of hypoglycemic coma, which were controlled by intravenous injections of dextrose solution. The patients were hospitalized in a state of severe precoma or in an advanced stage of hypoglycemic coma. Intravenous injections of hypertonic dextrose solution were not given to 3 patients, and they failed to benefit the other 3. Coma was constant for periods of 3 to 27 days. Autopsy showed cerebral arteriosclerosis in 4 patients and glomerulosclerosis in 2. An anatomicopathological study of the brains of the 4 patients who had had cerebral arteriosclerosis showed cerebral lesions characteristic of anoxia. The lesions were selectively located on the 3rd and 5th layers of the cortex, causing perivascular and pericellular edema, severe reactions of the macroglia and of the microglia, and destruction of the fibrils and axons of the deeper cerebral structures.

The authors believe that malnutrition, cerebral arteriosclerosis, and glomerulosclerosis were the causal factors of irreversible hypoglycemic coma. Tuberculous meningitis and yellow atrophy of the liver in one case may have been coadjutant causal factors. The authors advise caution in administering insulin to the elderly and to patients who are hospitalized as emergency cases with diabetic coma. They also advise determination of the glucose level of the blood before operating on diabetic patients. and before treatment for diabetic coma is given, for the purpose of deciding the advisability of either increasing or decreasing insulin dosage and of giving intravenous injections of dextrose solution.

Differential Diagnosis in Disseminated Pulmonary Infiltration. L. Ehrner and L. Hillenius. Nord. med. 63:79-86 (Jan. 21) 1960 (In Swedish) [Stockholm].

Diseases from various branches of internal medicine, which may be considered as causing disseminated, mainly small pulmonary changes, are tabulated. Roentgenologic diagnosis is uncertain. In the Karolinska Sjukhus, Stockholm, apart from the usual routine tests, the methods mainly followed in establishing the diagnosis are sternal puncture, electrophoresis, and cytological examination of sputum, pleural exudate, and lymph node punctate; there are also biological tests according to Daniels, muscle biopsy, and mediastinoscopy with test excision of paratracheal glands or glands in the hilus tract. On the patient's admission, serum is sent in for complement-binding reactions for fungi, and cutaneous tests for fungi are started. Bronchoscopy seldom gives direct information on disseminated pulmonary infiltrates. Bronchography should be done in case of suspected bronchiectasis. With thoracoscopy, suspected parts of the lungs can at times be more easily punctured for histological examination. Percutaneous aspiration biopsy from the lungs has been used more and more; the only complications have been pneumothorax and sometimes hemoptysis.

Arteriosclerosis Obliterans: Review of 520 Cases with Special Reference to Pathogenic and Prognostic Factors. J. L. Juergens, N. W. Barker, and E. A. Hines Jr. Circulation 21:188-195 (Feb.) 1960 [New York].

The Mayo Clinic records of 520 nondiabetic patients, under 60 years of age, with arteriosclerosis obliterans in the period 1939-1948 were reviewed from the standpoint of pathogenesis, prognosis, and clinical course of the disease. The findings were compared with 2 control groups, consisting of a total of 194 nondiabetic male patients, aged between 40 and 60 years, who had no clinical evidence of atherosclerosis of the coronary or the peripheral arteries. The ratio of male to female patients with arteriosclerosis obliterans was 11 to 1, and the mean concentration of plasma cholesterol in the male patients was about 50 mg. per 100 ml. greater than that of either of the 2 control groups. Only 12 male patients (2.5%) were smokers. The incidence of smoking among men in this series was higher than in the control groups. Twenty-six patients were obese (5%). Hypertension was associated with the disease about 3 times as often as in either control group.

The survival rate for patients with arteriosclerosis obliterans was less favorable than that of the normal population. The survival rate for patients with atherosclerotic aortoiliac occlusion was significantly less favorable than that of patients with atherosclerotic occlusion of the femoral artery. Disease of the coronary artery was probably the cause of death in about three-fourths of the patients who died. Twenty-one patients (4%) required amputation of a leg shortly after the diagnosis of arteriosclerosis obliterans was made, and an additional 4.9% required amputation during the 5-year period after the initial examination.

SURGERY

Infarction of the Descending Colon Due to Vascular Occlusion: Report of Three Cases. J. J. McCort. New England J. Med. 262:168-172 (Jan. 28) 1960 [Boston].

Three patients with infarction of the descending colon due to occlusion of the inferior mesenteric artery were observed by the author over a period of 9 years. In the first patient, a 51-year-old man, both legs had been amputated for gangrene, and a short time previously the patient had had a myocardial infarction. Because of his history of thromboangiitis obliterans, a vascular obstruction was suspected as the cause of the abdominal pain. At laparotomy the colon, from the midtransverse region to the rectosigmoid, was blue black, and there was severe inflammation in areas of the transverse colon. The inferior mesenteric artery was occluded by thrombus. Thirteen days after the operation the abdominal pain recurred. At reoperation, 2 areas of gangrene were found in the small intestine. These were resected, but the patient died after operation. In the second patient, a 76-year-old woman, the inferior mesenteric artery was occluded by a hematoma formed by a rupturing abdominal aneurysm. Necrosis of the intestine was indicated by the appearance on barium-anema examination. However, as her condition became too critical to allow definitive surgery, she died. The third patient, an 81-year-old woman, was seen early in the course of her illness, and on clinical grounds a mesenteric vascular occlusion was suspected. The fact that the intestinal wall in the splenic flexure was thickened, whereas the ascending colon was dilated, indicated, in retrospect, that the descending colon was infarcted. The patient was cured by prompt surgical resection.

The author points out that infarction of the descending colon due to inferior mesenteric vascular occlusion alone and without mechanical obstruction, such as volvulus or incarcerated hernia, is uncommon. Exclusive of those cases mentioned as part of a large series of mesenteric infarctions, the author found only 15 cases in the available literature. The relative incidence of infarction of the descending and the ascending colon has been estimated at about 1:40. One reason for the infrequency of infarction of the descending colon lies in the anatomy of the inferior mesenteric artery, which is shorter than the superior mesenteric and supplies a smaller intestinal segment. Abundant anastomoses exist between the middle hemorrhoidal branches of the hypogastric artery below. When these anastomotic vessels are intact, infarction of the colon is unusual.

Occlusion of the inferior mesenteric artery may produce no symptoms as long as the collateral circulation is adequate. Infarction of the descending colon has a more insidious onset than infarction of other portions of the colon. Since the descending colon is primarily concerned with the storage of fecal material before expulsion, it plays a less important part in the absorption of food and in the dynamics of fluid balance, and disturbances in its function are slower to appear. The onset of infarction is characterized by left-sided abdominal pain, loose bloody stools, abdominal distention, and progressive shock. It is accompanied by a rising white blood cell count. Radiographically, the infarced descending colon is contracted; gaseous distention tends to occur proximal to the involved segment; the wall is thickened and nodular, with multiple mucosal ulcerations; haustral markings are obliterated; and the involved segment is rigid and undistensible. Prompt recognition of the vascular accident is important, and immediate resection of the infarcted intestine is the treatment of choice.

Spleen in Thrombopenic Purpura. H. Oliva, A. Valle, and C. Jiménez Díaz. Rev. clín. españ. 75: 223-229 (Nov. 30) 1959 (In Spanish) [Madrid].

The favorable therapeutic effect of splenectomy in patients with chronic thrombopenic purpura is, as a rule, decisive. It is shown by an increase in the number of blood platelets, by the complete cessation of hemorrhages, and by improvement of the severe general symptoms. However, the appearance of transient periods of thrombopenia, without hemorrhages, is frequently observed in patients who have undergone splenectomy.

Sixteen spleens obtained from adolescent and adult patients with thrombopenic purpura were subjected to an anatomicopathological study. Fifteen of the spleens had been removed surgically; one was obtained during an autopsy. Macroscopically, all the spleens appeared to be normal, but they weighed less than normal spleens. The main anatomicopathological changes consisted of reticuloendothelial and lymphoid follicular hyperplasia of the type observed in spleens with hypersplenism. Depots of a substance positive to PAS were found present in hyperplasic lymph follicles. The authors believe that this substance inhibits maturation of the megakaryoblasts in the bone marrow, being the main factor in the development of thrombopenic purpura. The increase in the number of blood platelets after splenectomy shows the reaction of the bone marrow upon liberation of the splenic secretions. The transient periods of thrombopenia, which appear after splenectomy in patients who have had thrombopenic purpura, are due to temporary failure of the bone marrow to effect the favorable reaction.

Diagnosis and Treatment of Portal Hypertension. B. A. Petrov and E. I. Galperin. Khirurgiya 35:32-38 (Dec.) 1959 (In Russian) [Moscow].

The authors report on 84 patients who were hospitalized for portal hypertension during a 5-year period. Hemorrhage from veins of the esophagus was present in 54 patients. Thirty-eight patients were admitted with erroneous diagnosis, and unnecessary laparotomy was performed on 8 of them. Intrasplenic pressure was measured in more than 40 patients, and splenoportography was performed on 35 patients. These 2 procedures have been of great aid in the early diagnosis of portal hypertension. An intrasplenic pressure of more than 250 mm. H_2O is a good index of an associated enlargement of the veins of the esophagus and of an imminent hemorrhage.

Twenty-six patients received surgical treatment. Chronic ascites was the main symptom in 10 patients, and enlarged veins of the esophagus accompanied by hemorrhage in 16. All 10 patients with chronic ascites died after the operation, 8 of them at the hospital and 2 during the 1st year after discharge. Of the 16 patients with enlarged veins of the esophagus accompanied by hemorrhage, 3 died after the operation at the hospital, and 1 a long time after discharge. Direct portacaval end-to-side anastomosis afforded a stable decrease of portal hypertension and prevented possible occurrence of hemorrhage.

Comparative Evaluation of the Treatment of Perforating Ulcers of the Stomach and Duodenum by Simple Closure and Resection. L. V. Poluektov. Khirurgiya 35:11-17 (Dec.) 1959 (In Russian) [Moscow].

The author reports on immediate and late postoperative results in cases of perforating ulcers of the stomach and duodenum, 205 patients being operated on by simple closure and 71 by resection. There were 9 immediate postoperative deaths among patients operated on by simple closure and none among those who underwent resection. Six deaths can be attributed to belated hospitalization. Postoperative complications were more frequent, and the recovery period slightly longer, among patients operated on by simple closure than among those in the resection group. Resection was not any more hazardous than simple closure in this series, judging by the immediate postoperative results.

One hundred eighty-five patients, 130 of whom were operated on by simple closure and 55 by resection, were followed up for a period of 1 to 10 years. Of the patients who were operated on by simple closure, good long-term results were obtained in 42 (32.3%), fair in 28 (21.6%), and poor in 60 (46.1%). Of the patients who underwent resection, good results were obtained in 43 (78.1%), fair in 11 (20.1%), and poor in 1 (1.8%). The highest incidence of poor results was noted during the 4 years after operation. This study convinced the author that both immediate and late postoperative results are better after resection than after simple closure of perforating ulcers of the stomach and duodenum.

Homologous Artery Transplant in Obstruction of Aorta Bifurcation. B. L. Lindström. Finska läk.-sällsk. handl. 102:220-230 [no. 2] 1959 (In Swedish) [Helsinki].

A laborer, aged 33 years, with aortoiliac obstruction, who could walk only 50 meters, was treated surgically in February, 1959, by application of a homologous arterial graft from the arterial bank of the Maria Hospital in Helsinki. After thrombectomy of the abdominal aorta, a graft was applied as a bypass from the aorta to the right femoral and the left common iliac artery. On follow-up 6 months later, the patient reported that he could now walk freely. Aortography showed a functioning graft, the oscillogram was normal, and all peripheral pulses in the lower extremities were palpable.

Late Results of Surgical Treatment of Constrictive Pericarditis. G. G. Karavanov and Y. S. Valigura. Novy khir. arkh. 6:8-12 (Nov.-Dec.) 1959 (In Russian) [Kiev, Russia].

The authors report on 31 patients, aged between 5 and 50 years, with constrictive pericarditis, who received surgical treatment between 1949 and 1957. There were 23 men and 8 women. Tuberculosis was the cause of the disease in 25 patients. Ten patients died shortly after the operation. Late postoperative results were observed within a year in 3 patients, within 3 years in 4, within 5 years in 7, within 7 years in 5, and within 8 years in 2. Good postoperative results were observed in 16 patients, and fair results in 5. Most of the patients with good postoperative results regained their working ability. Edema and ascites disappeared within the 1st postoperative year. Diuresis and temperature became normal in most of the patients. The authors suggest early surgical treatment of patients with constrictive pericarditis. If pericarditis is associated with effusion, it is recommended that the effusion first be treated and that one then proceed with surgery.

The Association of Periodic Paralysis with Hyperthyroidism. S. W. Law, J. B. Rochelle III, and G. L. Jordan Jr. A. M. A. Arch. Surg. 80:181-186 (Feb.) 1960 [Chicago].

Periodic paralysis is a rare syndrome characterized by brief episodes of weakness or paralysis of skeletal muscles. A wider appreciation of periodic paralysis is warranted because of the occasional concurrent appearance of this syndrome with hyperthyroidism. Only 14 patients with this combination of periodic paralysis and hyperthyroidism have been reported in the United States. The authors present the 15th case, a 24-year-old Latin American college student who was first seen in January, 1957, when he complained of recurring weakness of his legs during the preceding year. The patient described episodes of extreme weakness of his legs, and less severe ones of his arms, which occurred about once weekly. Symptoms usually appeared in the early morning hours and gradually disappeared. Physical examination, including a neurological examination, revealed no abnormality. A diagnosis of myopathy of undetermined type was made. About 6 months later the patient complained of an increase in frequency and severity of the attacks, and stated that potassium chloride taken orally seemed to produce improvement in his symptoms. When he discontinued the potassium chloride therapy, the paralytic attacks became more frequent and severe.

A provisional diagnosis of periodic paralysis was made, and an attack was elicited by vigorous exercise. During this attack the serum potassium concentration was found to be reduced, but increased again as normal muscle strength returned. Later it was found that the patient had a fine tremor of the outstretched hands, and the thyroid was diffusely enlarged. A tentative diagnosis of hyperthyroidism with associated periodic paralysis was made. During preparatory treatment for thyroidectomy with the administration of methimazole (Tapazole) and potassium chloride supplements, reevaluation after 2 weeks revealed no recurrence of paralysis. Subtotal thyroidectomy was performed under general anesthesia. The surgical pathology report was hyperplasia of the thyroid gland, secretory and resting phases. This patient has been seen periodically since discharge, the last visit being on Feb. 3, 1959, 16 months postoperatively. At this time he was completely asymptomatic and clinically euthyroid. He has not experienced a paralytic episode since thyroidectomy.

From the data currently available, hypopotassemia due to sequestration of potassium within the body must be considered the basic physiological alteration of periodic paralysis, but the mechanism by which this occurs has not been satisfactorily delineated. The prophylactic administration of potassium salts has definite value in reducing the frequency and severity of the attacks. It appears that the hyperthyroid state precipitates the appearance of the episodic paralysis. Control of the hyperthyroidism has resulted in disappearance of the periodic paralysis in all the patients reported.

Severe Hemorrhage from Esophagogastric Varices: Its Emergency Management with Particular Reference to Portacaval Anastomosis. L. M. Rousselot, F. E. Gilbertson, and W. F. Panke. New England J. Med. 262:269-276 (Feb. 11) 1960 [Boston].

Emergency operative management of severe hemorrhage from esophagogastric varices has been under trial. Since follow-up studies have shown that 50 to 80% of the patients who recover from their 1st episode will not survive more than 1 or 2 years and that more than half of these late deaths will occur during subsequent hemorrhage, the problem is far from solved with the mere cessation of bleeding, unless this has been accomplished by a measure designed for permanent protection (that is, portacaval anastomosis).

Fifty-eight patients underwent emergency treatment for active hemorrhage from esophagogastric varices due to portal hypertension on the surgical service of St. Vincent's Hospital, New York, during the period from June 20, 1956, through Dec. 20, 1958. Cirrhosis was the cause in all but 2 patients (who had acquired portal vein thrombosis). Among the 56 patients with cirrhosis, the disease was associated with excessive intake of alcohol in 47 and with antecedent histories of viral hepatitis in 2. No obvious etiological factors were found in the remaining 7. Several patients who were initially admitted to other institutions have been included because they were transferred to St. Vincent's Hospital while still depending on the indwelling and inflated Sengstaken-Blakemore tube for arrest of hemorrhage.

With regard to management, the 58 patients have been divided into 4 groups. In the 6 patients of group A, hemorrhage continued in the presence of the Sengstaken-Blakemore tube. Four of these died in shock before an operation could be performed. Of the 2 patients who were operated on while still bleeding, one who had had bleeding from colonic varices recovered after an emergency portacaval shunt, while the other died of tracheobronchitis and bronchopneumonia due to hemolytic Staphylococcus aureus 12 days after the emergency portacaval shunt had arrested the hemorrhage.

In the 10 patients of group B, hemorrhage recurred after having been briefly arrested by pneumatic tamponade. One patient with prior splenectomy and acquired portal vein thrombosis underwent an emergency esophagogastrectomy during her 5th month of gestation and did well. One patient underwent transesophageal ligation only and died of hepatic decompensation during the postoperative period. The other 8 patients of group B underwent emergency shunting procedures (portacaval in all except for a single splenorenal shunt because of thrombosed portal vein). Five of the 8 patients survived, including 1 who had not benefited from an earlier transesophageal ligation. The remaining 3 died during the postoperative interval (2 of hepatic failure, and 1 of wound abscess with staphylococcic septicemia).

In the 24 patients of group C, through use of the Sengstaken-Blakemore tube hemorrhage was controlled during the immediate recovery phase (an arbitrary period of 7 days). The subsequent courses of the patients were as follows: Eleven were later operated on to prevent recurrence of bleeding (portacaval anastomosis in 7, splenorenal shunt in 1, makeshift shunt in 1, and esophagogastrectomies in 2). There were 2 postoperative deaths. The 9 survivors did not experience further bleeding.

In the 18 patients of group D, bleeding ceased spontaneously, without any tamponade or emergency surgery. Subsequently they were all subjected to elective portacaval anastomosis. Four died during the postoperative period. All but 1 of the 14 who survived remain alive and free from further hemorrhage. The authors conclude that the emergency and early applications of the portacaval shunt warrant continued trial.

Early Treatment of Stove-in Chest. N. R. Barrett. Lancet 1:293-296 (Feb. 6) 1960 [London].

A "stove-in chest" results from multiple rib fractures or from disruption of the costosternal cartilages; it is often complicated by other injuries, but its peculiar feature is paradoxical movement of the chest wall at the site of the fractures. The perfection of fast touring cars and the construction of modern motorways have made these injuries common, but few surgeons are, as yet, experienced in the emergency treatments that may be vital. The immediate procedures advocated by the author and purporting to control the dangerous effects of stove-in chest are simple. The battle that must be won during the first few hours after the chest injury has been sustained, and the position that must be held for subsequent days or weeks, is against anoxia and carbon dioxide retention. Strapping the chest wall and administration of morphine and of barbiturate sedatives are contraindicated. The use of Drinker-type respirators is bad, because they compress the flail chest wall. The following measures are recommended on admission of patients with respiratory embarrassment due to stove-in chest: Anesthetization of the patient straight away in order to achieve controlled respiration; examination of the patient in an attempt to assess the relative priorities of multiple injuries; elimination of the additional burdens of hemothorax, pneumothorax, tamponade, dilatation of the stomach, or diaphragmatic hernia by appropriate catheterization, sealed drainage, or suction; improvement of the efficiency and ease of respiration by tracheostomy, if necessary; institution of controlled respiration with the aid of a mechanical breathing machine in desperate cases; and control of pain by local injections of an anesthetic solution. Morphine should not be given unless, or until, efficient respiration is assured. If after tracheostomy it is decided that a mechanical breathing machine must be used, adequate apparatus and personnel must be available. A patient kept alive artificially in this way requires constant medical and nursing care, at least in the early days of treatment. The high mortality associated with stove-in chest is due to cardiorespiratory failure, and notably to anoxia and carbon dioxide retention.

Blunt Trauma of the Abdomen. G. L. Watkins. A. M. A. Arch. Surg. 80:187-197 (Feb.) 1960 [Chicago].

This is a survey of 141 patients with abdominal injuries caused by blunt trauma, admitted to the St. Louis City Hospital between Jan. 1, 1948, and Jan. 1, 1958. Of these injuries, 68% occurred in males, of whom 60% were under 30 years of age. Most of these injuries were a result of automobile collisions, though almost as many involved pedestrians who had been struck by vehicles. A large percentage of this pedestrian group were children. Trauma from falls was due mostly to persons falling down stairways or workmen falling off ladders or scaffolds. Many of the direct blows to the abdomen were sustained in fights.

Ruptures of the spleen were the most frequent injury; these occurred in 56 patients, the spleen alone being injured in 25 and the remaining 31 having associated injuries. There were 8 deaths among the 56 patients. The spleen is the abdominal organ most vulnerable to blunt trauma. There is no effective treatment other than splenectomy. There were 38 patients with contusions of the abdominal wall, of whom 6 had associated injuries; there were no fatalities in this group.

Gastrointestinal tract injuries are predominantly in the small intestine, and require immediate suture or resection. Of 14 patients with such injuries, 2 died. There were 6 patients with injuries of the liver and 1 with laceration of the cystic artery, necessitating cholecystectomy. The history, clinical signs of peritonitis, and varying degrees of shock were of primary importance in establishing the diagnosis. Five of the lacerations were in the dome of the right lobe of the liver, and 1 involved the inferior surface; 3 were sutured, and 2 were treated by packing. One of the patients with sutured lacerations died of further hemorrhage and liver necrosis. and one treated by packing died of associated injuries.

There were 4 pancreatic injuries, with no fatalities. The serum amylase value was elevated in each case. Of 8 patients with injuries of the kidney, 2 had contusions, and 6 had lacerations. Nephrectomy was performed on 5 of the patients with lacerations, and 1 of these died as the result of associated injuries. There were 10 patients with rupture of the bladder; all of them were operated on, but 6 died.

The evaluation of the history and of the clinical findings is the most important step in the diagnosis of blunt trauma to the abdomen. Leukocyte count, hematocrit reading, and serum amylase determinations should be done in virtually all cases. Roentgenologic examination of the abdomen should be performed whenever feasible. Peritoneal tap is used chiefly in cases in which the diagnosis is in doubt, or the semiconscious or unconscious state of the patient makes evaluation difficult.

Abdominal Visceral Injury Due to Nonpenetrating Trauma. J. D. Martin Jr., G. D. Perdue, and W. H. Harrison. A. M. A. Arch. Surg. 80:192-197 (Feb.) 1960 [Chicago].

Abdominal injuries constitute a major group of all types of massive trauma. This report is based on an analysis of 271 patients seen in the 10-year period from July, 1948, through June, 1958. The patients were treated on the surgical services of Emory University Hospital, Grady Memorial Hospital, and the Veterans Administration Hospital of Atlanta, Ga. There were 38 deaths, a mortality of 14%. Vehicular accidents accounted for 186 cases (with 32 deaths); falls, for 35; being struck by an object, for 17; blows, for 14; athletics, for 8; and industrial machinery, for 5. In 6 cases the mode of injury was unknown.

The diagnosis of the nonpenetrating abdominal injury is frequently difficult, especially in the patient with multiple injuries and unconsciousness. Hematological changes, radiographic examinations, and peritoneal aspiration are valuable adjuvants, but repeated clinical evaluations are most reliable in making the diagnosis. The prognosis for the most part is directly related to the magnitude of the injury, such as damage to multiple organs within the abdomen or combined extraabdominal injury. The over-all mortality for the latter group was 21.6%; in multiple abdominal wounds it was 38.8%; when only a single abdominal organ was injured, it was 2.8%.

The operative treatment must consist in a systematic exploration of the entire abdomen. This may be required in the presence of uncontrolled shock when continued bleeding is suspected. Control of bleeding is not always easy. Mesenteric bleeding may require ligations which impair the circulation of the intestines. Careful inspection is imperative after bleeding has been controlled, and, if there is any question of viability, resection of the intestine may be required. Retroperitoneal hemorrhage causes concern because of its magnitude, the development of a hematoma subsequent to retraction of the injured vessel, and the inability to control the bleeding. Damaged major vessels can sometimes be repaired or replaced, but smaller ones, such as the mesenteric branches, cannot be satisfactorily restored.

Submucosal Lipomas of the Colon: Experience with 12 Cases. S. F. Ochsner and J. E. Ray. Dis. Colon & Rectum 3:1-8 (Jan.-Feb.) 1960 [Philadelphia].

The authors report on 9 men and 3 women, between the ages of 45 and 75 years, with submucosal lipomas of the colon, who were observed at the Ochsner Clinic in New Orleans. The commonest complaints of these patients were indigestion, recurring abdominal pain, constipation, and weakness. Seven patients had some evidence of loss of blood, but in only one was the lipoma ulcerated and the presumed source of bleeding. Two patients had symptoms suggestive of intestinal obstruction, and in one an advanced stage of intussusception was observed. In 3 patients the lesion was asymptomatic, being discovered incidentally. Five of the 6 tumors of the sigmoid were visualized proctoscopically.

Next to adenomatous polyps, lipomas are the most common benign tumors of the colon. The symptoms are inconspicuous until the occurrence of complications, such as ulcer, bleeding, intussusception, or obstruction. Submucosal lipomas of the rectum or lower sigmoid present a distinctive proctoscopic appearance, and usually can be removed proctoscopically. Above the proctoscopic level roentgenologic examination is successful in revealing the presence of most lipomas. The radiolucent shadow of a submucosal lipoma is smoothly outlined, sharply defined, occasionally pedunculated, and often distinctive enough to suggest a diagnosis of lipoma. Surgical removal is the only satisfactory treatment.

Cancer of the Rectum. H. F. Harbitz. Tidsskr. norske laegefor. 79:1449-1451 (Dec. 15) 1959 (In Norwegian) [Oslo].

Most cases of cancer of the rectum are easily diagnosed by direct digital exploration. The cancer is accessible for radical surgical therapy. According to larger statistics, cancer of the rectum most frequently occurs in men. There are polypous papillomatous tumors and more often hard tumors with tendency to circular spread and stricture. Rectal cancer is not infrequently multiple; for example, there are 2 tumors of the same kind, one more advanced than the other. Larger and smaller polyps may be found in the rectum, with all transitions from benign to malignant forms. Most patients with cancer of the rectum are somewhat older persons with previously good digestion and regular defecation, who during the last months have noticed some mucus and blood with the feces and changed type of feces. The tumor is often advanced before it gives symptoms. Rectosigmoidoscopy is a supplementary examination, in no way equaling finger exploration. Roentgen-ray examination is also only a supplementary examination, mainly for the high tumors. General symptoms, anemia, and weakness occur chiefly in the advanced stages. In differential diagnosis benign infiltrations, sometimes in connection with thrombosing of hemorrhoids, are considered; also, rectal strictures of the noncancerous kind, mainly those of lymphogranuloma inguinale or lymphogranuloma venereum. Ulcerative colitis seems to be increasing in frequency; possible transition into cancer should be borne in mind. At present the best treatment for cancer of the rectum is total extirpation, with artificial anus.

Lest We Forget. A. H. Weiland. South. M. J. 53: 175-177 (Feb.) 1960 [Birmingham, Ala.].

This report is concerned with 847 previously unreported casualties observed by the author during the period of several weeks subsequent to the invasion of France on D-Day, June 6, 1944. During a study of several of these cases at the U. S. Naval Research Institute at Bethesda, Md., this type of casualty was called a "solid blast injury." However, in view of the fact that such injury was always produced by a force directed upward, it was felt that the term "vertical force injury" would be more appropriate. The enemy had placed in various strategic positions, such as at the entrance to various harbor installations, acoustic mines containing approximately 2,200 lb. of high explosive. The mine was attracted by the vibration of a turning propeller. The ensuing explosion, usually just forward of the propeller or somewhere near the fantail of the ship, produced severe injuries to the personnel within the various compartments and on the deck of such a vessel.

At Bethesda attention was called to the fact that many of those who received the most severe injuries were in a horizontal position at the time of the blast. In the early stages of the war, naval personnel were instructed to lie on the deck in a prone position when an underwater explosion was imminent. From a study of these casualties it is evident that it was suicidal to assume a prone or supine position on the deck during one of these occasions. In the production of these injuries 2 factors were involved: (1) the immediate effect of the explosion, which produced a sudden upward thrust of the deck; (2) the subsequent heave of the deck which followed the initial explosion by perhaps 15 to 20 seconds. The effect of the immediate blast was undoubtedly the more important of the 2 impulses. The smaller and lighter the vessel, the more damage was to be encountered, the greater the number of casualties, and the more severe the injuries.

Of the 847 casualties due to vertical force, many were of a minor nature and consisted of contusions of the feet, sprains of the knee, simple subcutaneous hemorrhages into the soft parts of the lower extremities, or simply exposure and immersion. In practically all cases in which surgery was performed on the lower extremities, a characteristic type of subcutaneous hemorrhage was encountered, which involved practically the entire subcutaneous circumference of both lower extremities, extending up to and above the knees. This subcutaneous area of hemorrhage was approximately 1 cm. in thickness and was apparently the result of the rupture of many capillary vessels in the subcutaneous tissues. There were many patients with disturbances of the knees, probably due to a stretching or tearing of the collateral and cruciate ligaments. Then there were tibial plateau fractures of relatively mild degree. This fracture involved one or both tibial condyles.

In the class of more severe injuries were the multiple fractures of the feet, with penetration of the lower end of the tibia through the tarsus and several penetrations through the soft tissues of the sole of the foot. There were 17 casualties with complete dislocation of the knee; 3 of these were bilateral. Of the total number of knees dislocated, 4 dislocations were compound, with the femoral condyles protruding through the popliteal space; they were about evenly divided between anterior and posterior dislocations. Nineteen of these extremities were sacrificed because of gangrene. There were 98 casualties with compression fractures of one or more vertebrae; the greatest number of segments injured in any one person was 5.

The Unique, Accessible and Useful Plantaris Tendon. W. L. White. Plast. & Reconstruct. Surg. 25:133-141 (Feb.) 1960 [Baltimore].

The plantaris muscle with its long slender tendon is subject to considerable variation. It is a vestigial structure, and the use of its tendon in surgical reconstruction has been suggested by several investigators. Usually the plantaris muscle arises along the distal portion of the linea aspera of the femur and from the posterior ligament of the articular capsule of the knee. Its tendon is flat, narrow, and about 3 or 4 times as long as the fleshy part. The tendon traverses the leg distally, passing medially between the soleus and the overlying gastrocnemius muscles. Distally the tendon lies on the medial aspect of the Achilles or calcaneus tendon and inserts into the dorsal surface of the calcaneus and adjacent fibrous tissues. The insertion of the plantaris is highly variable, and it may be absent, agenesis having been observed in about 7% of 2,650 extremities studied.

In discussing surgical approaches to the plantaris tendon, the author says that several times he used a Masson 2-piece fascia stripper to obtain a plantaris tendon through a single incision made at the lower medial surface of the Achilles tendon, and that Brand has devised a light tendon stripper with a cutting edge that is most efficient in removing the plantaris and palmaris tendons through single distal incisions. To obtain the plantaris tendon, an incision, approximately 1 in. long, is made on the medial aspect of the Achilles tendon about 1 in. proximal to its insertion into the calcaneus. By means of a small hemostat the tissue is opened, and the Achilles tendon exposed; then, with the aid of retractors the plantaris tendon may be located. The tendon of the plantaris should be cut near its insertion into the calcaneus. The tendon end is passed through the loop of the tendon stripper and grasped with a Kocher clamp. The clamp is turned one full turn to wind up the tendon and permit a more secure grasp. The tendon stripper is then forced up the leg. The knee should be kept fully extended when the stripper is passed. The plantaris tendon possesses certain characteristics that greatly increase its usefulness for tendon grafting in hand reconstruction, and it may be used wherever fascial strips have been of value.

NEUROLOGY & PSYCHIATRY

Fractional Encephalography in a Study of Cerebral Tumors: Diagnostic Value. E. Díaz y Gómez, A. Rabano Navas, M. Gil Gayarre, and A. Colodron Alvarez. Rev. españ. oto-neuro-oftal. 18:375-378 (Nov.-Dec.) 1959 (In Spanish) [Valencia, Spain].

Seventy-five patients with cerebral disease were observed on the neurosurgery ward of the Hospital Provincial de Madrid. The patients had a fractional encephalography with the classical technique. The plates were obtained after the injection of 35 cc. of air and withdrawal of a certain quantity of cerebrospinal fluid. Out of a total number of 78 encephalograms made, 28 were normal and 50 were pathological, the latter including 13 encephalograms of 12 patients with cerebral tumors. In this group of 12 patients, the test was discontinued in one patient because of the occurrence of acute vomiting, in another because of the appearance of aggravated symptoms of a metastatic frontal tumor, in a 3rd patient because of the occurrence of decerebrate rigidity during the taking of the plates, and in a 4th patient because of the occurrence of acute cyanosis for 3 minutes during the start of induction of general anesthesia with thiopental (Pentothal) sodium. The 2 patients who suffered serious accidents immediately before and during the test died 1 day and 4 days, respectively, after the test. An autopsy on the patient who had decerebrate rigidity confirmed the encephalographic diagnosis of right temporal glioma deeply located. In the patient who had acute cyanosis immediately before the test, the histological study of a tumor removed at autopsy showed parietal glioma with involvement of the corpus callosum. In the remaining 8 cases, fractional encephalography was of value for the diagnosis of the location (intracerebral or extracerebral) of the tumor and for the determination of its nature. In 3 cases in which the circulation of air was deficient, the diagnosis was confirmed by angiography, which was made immediately after fractional encephalography. In a patient with a largely infiltrating frontoparietal glioma, both fractional encephalography and angiography failed. A definite diagnosis was made by the results of a 2nd fractional encephalography which was made 2 weeks after the 1st.

Changes in the Brain Associated with Senility. K. M. Wahal and H. E. Riggs. A. M. A. Arch. Neurol. 2:151-159 (Feb.) 1960 [Chicago].

The authors believe that disorders in systemic circulation might exert sufficient influence upon cerebral blood flow, even in the absence of stenosis of cerebral vessels, to result in neural dysfunction. Tangible support of this hypothesis was obtained by studying the anatomic substrata in the brains of such patients and by comparing them with the brains of younger patients with similar cardiac status. Autopsy records of 35 patients treated at the Philadelphia General Hospital were reviewed. Fifteen of the 35 patients, with an average age of 72 years, exhibited senile deterioration. The contratest group consisted of 12 adult patients, with an average age of 44 years, and 8 children, with an average age of 8 years, all with cardiac defects.

Inspection of specimens in the senile group showed surprisingly mild macroscopic alterations, in view of chronological age and degree of neurogenic deficit. Moderate widening and deepening of cortical fissures were observed, but advanced degrees of convolutional atrophy were absent. Ventricular dilatation, limited to the anterior horns of the lateral ventricles, was present in 8 brains. Thickening and opacity of the leptomeninges over the vertex and over the convexity of the hemispheres occurred in more than half of the specimens. Atheromatous plaques were present on basal arteries in 10 brains, but in no instance did they encroach upon the lumen. Comparable degrees of convolutional atrophy were present in 2 specimens obtained from the adult patients with cardiac defect. Meningeal fibrosis occurred in 4 adults of this group and in 3 of the juvenile group. Focal atheroma could be demonstrated in 4 adult and 2 juvenile specimens.

In contrast to the meager gross changes in the senile brain, degeneration at the cellular level was severe and widespread. Specimens were characterized by (1) disturbance of cytoarchitecture, incident to neuronal destruction and reactive gliosis; (2) lipid accumulation in neurons; and (3) regressive changes of small blood vessels within the brain substance. Alterations of cytoarchitecture were present throughout the neuroaxis, without affinity for any particular area. Lesions occurred as diffuse, poorly defined foci or, less frequently, as small, sharply defined areas, both characterized by patchy or confluent destruction of neurons. Parenchymatous degeneration occasioned no glial response in some locations, but, in general, was associated with astrocytic hyperplasia, often to the degree of obscuring the normal tissue pattern. Circumscribed lesions at times assumed the appearance of microinfarcts, with proliferated capillaries and activated microglia cells, in addition to hypertrophied astrocytes. The process was most easily identified in areas with distinctive structure, such as the cerebral cortex and the inferior olivary and dentate nuclei. Cortical involvement was always extensive, but not uniformly distributed or confined to specific topographic locations.

Essentially the same pattern of cerebral degeneration could be demonstrated in cardiac patients, both juvenile and adult, differing only in the extent and intensity of the process. The presence of similar brain lesions in younger persons without overt psychological disturbances suggests that functional disability may not depend directly upon neuroanatomic alterations, and may, therefore, be subject to arrest or reversal. In view of the relation of functional integrity of the nervous system to the nutritional and dynamic efficiency of its blood supply, attention to the physical status of the patient may offer a practical approach to the prevention of intellectual deterioration in the senium.

The Great Cerebral Arterial Currents: Anatomic Investigation and Deductions on the Pathogenesis and Location of Cerebral Hemorrhages. G. Lazorthes, J. Poulhes, G. Bastide, J. Roulleau, and F. Amaral-Gomes. Presse méd. 68:137-140 (Jan. 27) 1960 (In French) [Paris].

Two great and independent arterial currents flow through the brain—a peripheral and a central arterial network. The authors' hypothesis is that each type of short, medium, or long artery branches out on different planes of the cortex, ending at different cellular layers. The anatomic analysis of the peripheral network shows that the arteries in the white cerebral substance converge toward the lateral ventricle, and that their distribution and direction do not depend on the distribution and direction of the great vessel bundles which cross the white substance. The arterial vascularization of the great interhemispheric commissures presents some peculiar, little-known features. The corpus callosum has a more abundant vascularization than is generally believed, being crossed from end to end by the arteries from the cortical network, which give rise to numerous collateral vessels ending in fine, deep ramifications. The cerebral trigone is vascularized by the choroid arteries. The anterior choroid sends out numerous arterioles to the posterior pillars of the trigone and to the cornu Ammonis where there exists an amazingly rich vascularization.

The central arterial current of the brain is composed mainly of the arteries from the basal portion of the 3 great cerebral arteries and from the anterior and posterior communicating arteries. These 2 arterial groups vascularize the central nuclei. The anatomic analysis of the 2 great cerebral arterial systems shows that there exists, between the peripheral and the central current, a frontier area at which level 2 hemodynamic systems, each with a different structure, are juxtaposed but not anastomosed. The authors believe that this frontier plane, situated between 2 great nonanastomosed vascular systems of such different structures, represents a weak point in the cerebral arterial system, as a result of the difference in pressure between them. This neutral area, where pathological conditions may exist, is the preferred locale for cerebral hemorrhages, as Charcot had already ascertained.

The Happy College Student Myth: Psychiatric Implications. M. L. Selzer. A. M. A. Arch. Gen. Psychiat. 2:131-136 (Feb) 1960 [Chicago].

A diagnostic survey of all the students seen by 3 psychiatrists at the mental hygiene clinic of the University of Michigan revealed nosological information somewhat contrary to expectation. Referral sources varied, but the self-referred accounted for approximately 40%. Physicians referred 29%, and 9% were referred by the faculty. The remaining 22% were referred by deans, dormitory staff members, and academic counselors. Of 506 students interviewed by the psychiatrists on the clinic staff, 35.4% were psychoneurotic, 24.5% had personality disorders, and 21.7% were schizophrenes. Adjustment reactions comprised only 8.3% of the disorders noted. Thus, 81.6% of the patient group fell into the 3 major psychodiagnostic categories. The diagnostic data, when compared with previously published data, suggest that the conditions of students seen at college mental hygiene clinics may be underdiagnosed. The author believes that such patients are diagnostically comparable to those encountered in any outpatient psychiatric clinic accessible to the general public.

GYNECOLOGY & OBSTETRICS

Surgical Treatment of Stage 1 Cancer of the Cervix. A. Brunschwig. Cancer 13:34-36 (Jan.-Feb.) 1960 [Philadelphia].

This report is concerned with the results of a surgical program for cancer of the cervix pursued at the Memorial Center for Cancer and Allied Diseases in New York since 1947. Only patients with stage 1 cancer are included in this report. The stage was recorded at the 1st examination. Microscopic studies on the surgical specimens sometimes revealed that the cancer had invaded the parametrium or the vaginal fornix, so that the cancer was really in stage 2, although the original impression had been of a stage 1 lesion. Operations envisaging "cure" were performed on 153 of 177 patients admitted with stage 1 cervical cancer between September, 1947, and December, 1953. Radical panhysterectomy and excision of the pelvic lymph nodes was the procedure of choice and was performed on 132 patients. A Schauta type of radical vaginal procedure was performed on 9 poor-risk patients; total hysterectomy, on 10 patients; and a "classical Wertheim" operation, on 2 patients. In tabulating the results, 4 patients had to be excluded, 2 because they were lost to follow-up before 5 years had elapsed, and 2 because they died after 3 and 4 years, respectively, of conditions not related to cervical cancer. Of the remaining 149 patients, 124 (83%) were alive 5 years later. Among the 104 patients who had macroscopic lesions, varying in size from 5 mm. to involvement of all the cervix or endocervix, and who were free from node metastases, the 5-year salvage rate was 87%. Among those with pelvic node metastases, the 5-year salvage rate was 50%.

Iron-Deficiency Anemia in Pregnancy. C. A. Hunter Jr. Surg. Gynec. & Obst. 110:210-214 (Feb.) 1960 [Chicago].

Among 4,744 consecutive patients admitted to the obstetric service of the Indiana University Medical Center, Indianapolis, during the period from 1956 to 1958 inclusive, 852 patients were found to have moderate anemia, and 89 severe anemia. In this series moderate anemia refers to a hemoglobin level ranging from 9 to 11 Gm. per 100 ml., and severe anemia to a level of less than 9 Gm. per 100 ml., occurring at any time during the prenatal period. Approximately one-third of these patients are from the private service, and two-thirds from the ward service. The over-all incidence of moderate and severe iron-deficiency anemia was 20%, of which 2% was severe anemia. Reports by other investigators and observations during this study indicate that a level of 12 Gm., rather than 11 Gm., per 100 ml. should be the dividing line. The author discusses various aspects of the metabolism of iron in pregnant women, commenting on its absorption from the diet, transport in the plasma, storage, role in erythropoiesis, and excretion, as well as the transport of iron to the fetus.

To stress that iron is required for the treatment of iron-deficiency anemia may seem trite, but the author considers it necessary in view of the vast number of multiple "hematinics" offered to the physician. To date, there has been no clear evidence of the increased efficacy of iron salts in a combination of vitamins, specifically vitamin B_{12} and folic acid. Cobalt in combination with iron may induce an increase in the hematocrit, but the difference in this hematocrit reading over that produced by iron salts alone is not important. Several clinicians believe that cobalt has no place in the treatment of iron-deficiency anemia. It has been demonstrated that persons with gastric achlorhydria absorb iron normally, and, as a result, these patients do not need hydrochloric acid or ascorbic acid to supplement the iron therapy.

Iron is the proper treatment for iron-deficiency anemia. It can be given orally or parenterally, but the oral route is to be preferred. The orally administered salts, ferrous sulfate and ferrous gluconate, are still unsurpassed in both effectiveness and low cost. From 10 to 15% of the iron is absorbed when given in amounts of 80 to 150 mg. per day. Larger sources of orally administered iron will not materially increase its absorption and will be likely to cause irritability of the gastrointestinal tract. The chief indications for the parenteral administration of iron in the prenatal period are intolerance to orally given iron or a limited time for correcting the iron deficit before the onset of labor.

Primary Ovarian Pregnancy: Report of 2 Cases. R. I. Breuer. Am. J. Obst. & Gynec. 79:255-258 (Feb.) 1960 [St. Louis].

The author believes that ovarian pregnancy might not be as rare as is widely believed. He presents 2 cases that were observed in February, 1957, and January, 1958, respectively, at the University Hospitals of Cleveland. These 2 cases illustrate the difficulty in distinguishing ovarian from other forms of ectopic pregnancy. The predominant features in both cases were lower abdominal pain and abnormal vaginal bleeding. The surgical findings in the 1st patient completely satisfied the rigid criteria established by Spiegelberg in 1878 for the diagnosis of primary ovarian pregnancy: "the tube intact and separate from the ovary, the gestation sac and ovary in the normal ovarian position, the ovary connected to the uterus by the ovarian ligaments, and the microscopic demonstration of ovarian tissue in the wall of the gestational sac." In the 2nd patient the tube could not be plainly identified and grossly separated from the ovary. Therefore, tubo-ovarian gestation cannot be ruled out, but this is only negative evidence. The fact that this gestation progressed to viability and the fetal sac structures to a 28-week size, plus the microscopic presence of the uterine tube and the failure to demonstrate evidence of microscopic invasion of the tube or other structures by embryonic tissues, provides strong evidence that the pregnancy was ovarian in site and represents but a progression of the pathological findings observed in the 1st patient.

Eclampsia Without Convulsions: Eclamptic Lesions in Fatal Maternal Cases with and Without Clinical Pre-Eclampsia. P. J. Stein, A. J. Kobak, P. B. Szanto, and G. Moran. Am. J. Obst. & Gynec. 79:266-278 (Feb.) 1960 [St. Louis].

In considering whether or not convulsions are part of the clinical picture of severe toxemia, the authors point out that in the United States the presence of convulsions in toxemia of pregnancy has served to demarcate those cases which are more severe or fatal from those which are less severe and nonfatal. The presence of convulsions is generally taken to mean eclampsia and possible death, whereas their absence connotes preeclampsia and less likelihood of death. How, then, does one classify the patient who dies with autopsy evidences of eclampsia, even though convulsions have not occurred? This confusion in nomenclature has been responsible for the adoption of the term "eclampsia without convulsions," which has been invariably an autopsy diagnosis. The authors reviewed the autopsy material at the Cook County Hospital in Chicago from 1946 to 1955 and found 7 cases in which the pathological findings indicated eclampsia on the basis of Sheehan's criteria. From the fact that during the period in question 88,690 deliveries took place at the hospital, the authors deduce that the entity occurs about once in every 12,670 deliveries, an incidence of 0.008%. Eclampsia with convulsions occurred once in every 452 deliveries, an incidence of 0.2%. The ratio between these 2 types of eclampsia was thus 1:28.

The histories of the 7 patients are presented, and the authors comment on the lesions observed in the liver, kidney, and brain, and suggest that further liver and kidney biopsy studies may eventually help to establish a relationship between the pathological lesion and the clinical entity. They mention the relationship between convulsions and cerebral dysrhythmia and point out that convulsive seizures, even in the presence of toxemia, do not necessarily verify the diagnosis of eclampsia. The severity of some of the pathological changes in patients with clinical preeclampsia shows that convulsions serve a beneficial function in calling forth decisive action quickly. Moreover, since definitive treatment is often delayed by a conservative therapeutic attitude whenever a diagnosis of preeclampsia is made, a more careful evaluation and appreciation of the severity of the condition is necessary to avoid a fatal outcome, even though convulsions have not yet occurred.

Fetal Death Before the Onset of Labor: An Analysis of 407 Cases. D. J. Grandin and R. E. Hall. Am. J. Obst. & Gynec. 79:237-243 (Feb.) 1960 [St. Louis].

During the decade 1944-1953 there were born at the Sloane Hospital for Women in New York 34,368 babies with weights exceeding 500 Gm. (1 lb. 2 oz.). Of these, 407 (1.2%) died before the onset of labor. The authors review the data on these 407 fetal deaths. Of the mothers, 173 were nulliparous, and 234 were parous. Among the 234 parous women 50 (21%) had had previous stillbirths: 42 had had 1 previous stillbirth, and 8 had had 2. Nineteen of the 50 patients had Rh incompatibility, 6 had anomalous progeny, and 5 were diabetic; the remaining 20 cases of repeated stillbirth could not be related to any condition which is thought to be associated with repetitive fetal loss. Maceration was present in 309, absent in 59, and not recorded in the remainder of the 407 stillbirths.

The fetal deaths are tabulated according to causation in 10 groups. No cause could be found for the fetal death in 113 (27.8%) of the cases. Toxemia of pregnancy and allied conditions were thought to be the cause of death in 106 (26%) of the fetuses. Premature separation of the normally implanted placenta was responsible for 58, and congenital anomalies and/or polyhydramnios for 45 of the fetal deaths. Erythroblastosis was observed in 36, and cord accidents in 27 cases. Diabetes or sickle-cell anemia was found in the mothers of 14 of the stillborn infants. Amnionitis, associated with premature rupture of the membranes, was thought to be responsible for 4 deaths. In one case external version at term was followed by loss of the fetal heart tones and delivery of a macerated fetus 7 days later. Although fetal death occurred after the 41st week in 16 cases, analysis revealed that in only 3 of these was postmaturity the only factor responsible for death.

When intrauterine fetal death is discovered, one cannot predict when the conceptus will be expelled. It has been stated that, regardless of when a fetus dies in utero, delivery will rarely be delayed beyond the estimated date of confinement. This was substantiated by this study. Of the 200 fetal deaths which occurred prior to the 38th week, delivery was delayed beyond the 40th week in only 2. Of the 107 fetuses whose deaths occurred after the 37th week, only 6 were delivered more than 2 weeks later. The greatest interval between fetal death and delivery was 90 days (following death due to erythroblastosis at 30 weeks). There were 22 instances in which the interval exceeded 4 weeks, 8 in which it exceeded 6 weeks, and 4 in which it exceeded 8 weeks. In general, the interval between fetal death and the onset of labor was found to be inversely related to the gestational age of the fetus at the time of its death. The incidence of puerperal morbidity and of postpartum hemorrhage was increased in stillbirths. Management was essentially conservative. Oxytocics, amniotomy, and cesarean section were employed.

With regard to hypofibrinogenemia in association with fetal death in utero, the authors point out that this syndrome was not well known during the period reviewed, but there was no maternal death in these 407 cases, and only one of the mothers received more than 1,000 cc. of blood. From this the authors deduce that this syndrome may be, if not rare, at least far less dangerous than some recent reports have indicated.

PEDIATRICS

The Role of Splenectomy in the Management of Thalassemia. C. H. Smith, M. E. Erlandson, G. Stern, and I. Schulman. Blood 15:197-211 (Feb.) 1960 [New York].

Of 58 children with severe thalassemia (Cooley's anemia), who attended a special out-patient transfusion clinic of the New York Hospital–Cornell Medical Center in the past 26 years, 29 had been subjected to splenectomy. Data were obtained from these patients over a postoperative period ranging from 5 months to 9 years. The postsplenectomy observations showed that splenectomy eliminates the extracorpuscular mechanism responsible for the accelerated destruction of normal donor red blood cells in the patient's circulation. This represents a lasting improvement and accounts for an increased longevity of normal blood supplements and a striking reduction in transfusion requirements. Less blood was required to maintain at least as good, and at times improved, hemoglobin levels. Estimates of duration of survival of the patient's own erythrocytes suggest that the basic hemolytic defect is not altered significantly by splenectomy. While transfusions and splenectomy promote the patient's well-being, growth in height and sexual development are retarded. Secondary sexual characteristics develop, if at all, later than in normal persons, and normal menstruation is rare.

Cardiac failure occurred in 10 patients; all but one had been subjected to splenectomy. This group was characterized by cardiac enlargement, multiple arrhythmias, and death from refractory heart failure, usually in the 2nd decade of life. Cardiac complications are likely to be related to the heavy deposition of iron in the myocardium, and are comparable in this respect to a similar incidence in idiopathic hemochromatosis. One of the most serious problems in the management of thalassemia is the prevention and control of congestive heart failure. This will depend on the discovery of an effective method by which the heart can be made to unload its iron deposits. The increased susceptibility to infection after splenectomy in patients with severe thalassemia indicates that the normal immunological responses inherent in the spleen remain intact despite the stress of a continuous hemolytic process.

Two Cases of Nuclear Icterus in Newborn Infants with Erythrocytic Enzymatic Defect. G. Segni. Minerva pediat. 11:1420-1426 (Dec. 15) 1959 (In Italian) [Turin, Italy].

The cases of 2 newborn infants with severe nuclear icterus and erythrocytic defect in the activity of glucose-6-phosphate dehydrogenase are reported. Both babies presented acute symptoms and died in less than 24 hours after the onset of the disease. Results of laboratory tests were similar in the 2 cases. There was no blood incompatibility between the mother and the fetus; immunohematological tests were negative. There was no erythroblastosis of the peripheral blood, although histological examination showed some extramedullary erythroblastosis. Heinz bodies were found in both cases. The author points out that the mother of the 1st baby had taken some tablets of an analgesic antineuralgic preparation during the 1st 48 hours after delivery. There have been no reports so far on the possible hemolytic effect of the preparation taken by the mother, but knowledge of some incidents of thrombopenia in babies born to mothers treated with this preparation may be revealing for the diagnosis. The 2nd baby had received 10 mg. of vitamin K. It is known that this vitamin may cause a slow hemolysis in premature babies, but in the infant reported death was immediate, and, moreover, the dose of vitamin K was small. The author believes that nuclear icterus and erythrocytic deficiency of glucose-6-phosphate dehydrogenase may be suspected in the absence of an indication of blood incompatibility when the family history is negative for favism, or simply may be suspected in certain regions where the incidence of the enzymatic defect is high.

Cerebral Palsy in Manitoba. J. K. Martin. Canad. M. A. J. 82:411-417 (Feb. 20) 1960 [Toronto].

The author reports on 207 boys and 163 girls, between the ages of less than 2 and 17 years, with cerebral palsy, who were studied under the auspices of the Society for Crippled Children and Adults of Manitoba. The highest incidence of the disease was found in children between the ages of 5 and 9 years, with 1.574 cases per 1,000. One should remember that in certain countries the incidence is often given as per 100,000 population, which explains the differences between these data and those reported by other workers. Diagnostic classification revealed that 272 (73.6%) of the 370 children were spastic, and among these the patients with right hemiplegia formed the majority.

In the search for a causative factor, premature birth was the abnormality most frequently observed. Among the acquired lesions, encephalitis (and particularly western equine encephalitis), cranial trauma, and meningitis were observed in several patients. Anoxia was considered to be a factor when the history revealed cyanosis at birth, prolonged labor, fetal damage, or other causes which may have suggested an oxygen deficiency. In 22 patients (5.9%) Rh incompatibility was the only detectable causative factor. The term "familial" was employed to characterize this disorder if more than one child in the same family was affected. Nineteen pairs of twins were observed among the 216 patients with so-called congenital cerebral paralysis. This incidence of 8.7% is nearly 8 times the normal. Twenty-five patients with cerebral palsy had associated anomalies, such as hydrocephalus, congenital dislocation of the hip, congenital heart lesions, microcephaly, absence of the septum pellucidum, congenital deformity of an arm, precocious puberty, congenital absence of the sacrum, congenital anomalies of the kidneys, subdural hygroma, porencephalia, cataract of one eye, and hemangiomatosis.

The intelligence quotient of 33% of the patients was less than 70; 25.8% had an IQ between 70 and 89; and 41.2% had an IQ above 90. About 40% of the patients were able to attend regular schools, while 30% required special educational facilities. It was estimated that facilities for intensive therapy would be necessary for about 35% of the patients, while another 35% might require little or no therapy. Fifteen per cent might be better placed in schools for retarded children, and 15% at some time during their lives might require institutional care. The most optimistic estimate would not place more than 60% of the children in a category likely to achieve financial independence as adults.

Interstitial Pulmonary Emphysema, Pneumomediastinum and Pneumothorax in Neonatal Period: Remarks on Application of Artificial Respiration in Asphyxia Neonatorum. E. Ryssing. Ugesk. laeger 122:31-35 (Jan. 14) 1960 (In Danish) [Copenhagen].

Two cases of neonatal pneumothorax are described. The pathogenesis, frequency, symptoms, and treatment of interstitial pulmonary emphysema, pneumomediastinum, and pneumothorax in the neonatal period are reviewed. The change in pressure which may normally occur at the start of spontaneous respiration can cause alveolar rupture if there are larger alveolar ectasias, because considerable parts of the lung present a substantial resistance to unfolding or because collected mucus acts as a valve. Under the same conditions artificial respiration with either positive or negative pressure can cause alveolar rupture, even if the pressure is kept within normal limits. If the pressure is increased to overcome the resistance presented by atelectatic or immature lungs, the risk is increased. On simultaneous lessening of the duration of the pressure, the artificial respiration is tolerated better, but the safety margin is probably narrow.

UROLOGY

Disturbances of the Dynamics of the Ureter After Plastic Operations on the Ureter with Interruption of Continuity. H. K. Büscher and A. Gaca. Chirurg 31:70-73 (Feb.) 1960 (In German) [Berlin].

The authors report on 8 men and 6 women, between the ages of 34 and 59 years, who underwent plastic operations on the ureter with interruption of continuity at the urologic clinic of the University of Homburg, Saar, Germany, in the course of the last 4 years and who were subjected to follow-up examinations regularly. Of the 14 patients, 7 underwent ureteroneocystostomy, 4 had a Boari plastic operation performed, and 3 underwent resection of the ureter with end-to-end anastomosis. The indications for these types of surgical intervention were specific and unspecific stenoses of the ureter, cicatricial changes associated with incarceration of calculi, and injuries of the ureter resulting from gynecologic interventions. Postoperative urograms and urograms taken later at greater intervals showed a regression of the dilatation of the ureter within 1 or 2 months in patients who had undergone ureteroneocystostomy or a Boari plastic operation, and within 12 to 20 months in patients who had undergone resection of the ureter in the third nearest to the kidney. Later a dilatation of the ureter and a disturbance of the peristalsis could not be observed any more. These findings suggest that the tendency of the postoperative atony of the ureter toward restoration of a normal tone is better the deeper the interruption of the ureter has been. Vesicoureteral reflux seems to be rare even with the most simple method employed for ureteroneocystostomy. No stenosis was observed at the uretero-ureteral anastomosis and at the vesicoureteral point of union.

The postoperative complications after a ureteral plastic operation with interruption of continuity are less in the line of risk of stenosis or reflux, but rather in that of disturbance of the dynamics of the ureter. Under aseptic conditions a complete return to health is possible. The postoperative danger is that disturbance in transportation of the urine favors the occurrence of pyelonephritis. Continuous drainage of the ureter does not have to serve as a "splint," but it has to secure the passing of urine as long as possible, at least during the 1st phase of the postoperative disturbance in transportation. Urinary infection requires not only postoperative but also prolonged treatment of the infection.

Vesicoureteral Regurgitation in Children. J. H. McGovern, V. F. Marshall, and A. J. Paquin Jr. J. Urol. 83:122-149 (Feb.) 1960 [Baltimore].

The authors report on 88 children, aged less than 14 years, with vesicoureteral regurgitation (reflux); 82 of these patients had definite urinary symptoms, 84 had pyuria, 81 had hydronephrosis of a degree more than barely detectable, 84 had had at least one attack of fever accompanied by pyuria and other indications of urinary origin, and 22 of the 56 in the group tested for a vesical residuum had over 50 cc. When followed for 6 months or more, not one of these 88 children with regurgitation continued without some of the following significant abnormalities: urinary symptoms, pyuria, hydronephrosis, vesical residuum, or clinical attacks of urinary infection. All the children thus had significant urinary abnormalities besides regurgitation. These findings and the fact that vesicoureteral regurgitation has been found only rarely, if at all, in normal children suggest that regurgitation can be considered a useful sign of urinary abnormality, and a test for regurgitation is usually an important part of a diagnostic study in children.

Of the 88 children with regurgitation, 43, with 86 ureters, were studied by inserting a catheter and by injecting the bladder rapidly to obvious fulness with a piston syringe by means of a distending, nonirritating, radiopaque fluid. This technique proved to be a practical method for showing regurgitation. The 43 children were followed for 6 months or more, cystograms being made 6 or more months after the 1st demonstration of the presence of regurgitation. The results showed that instances of regurgitation are not all etiologically the same. Some children had mainly vesical outlet obstruction; some had obstruction primarily at, or in the lowermost portion of, the ureters; some had the megacystis syndrome; and a few had frankly neurogenic bladders. Different stages of progression were observed in patients with the same fundamental causation. Although the children's basic anomalies themselves were not intrinsically progressive, the disease, as a whole, usually was. The elements of obstruction aid and abet one another at variable rates.

Vesicoureteral regurgitation in children is a reliable sign that the urinary tract is abnormal. Although the abnormality is sometimes transient and/or easily corrected, the prognosis tends generally toward the unfavorable. The rate of unfavorable progression varies greatly not only in different patients but often even in the same patient. Patients with reflux associated with changes in the upper urinary tract are dying but at different rates. Regurgitation is of itself abnormal and unfavorable. Correction of regurgitation is desirable, but the mere disappearance of this phenomenon is frequently insufficient to restore the urinary tract. Evidently, naturally occurring regurgitation is only a part of an undesirable anomalous complex, but it is an important part from both diagnostic and therapeutic considerations. Although nonsurgical management may sometimes stay the course, or rarely produce major improvement in patients with the fully developed condition, fundamental and apparently permanent restoration is achieved only by surgical intervention.

Detailed diagnosis is essential in planning a safe program. Diagnosis includes recognition of those circumstances in which damage is already so great that there is no reasonable prospect of major success; in this case prompt maximal drainage without foreign bodies is usually the treatment of choice. After deciding on a restorative program, the authors incline to progressing in stages from the top down: for example, nephrostomy, correction of ureteral obstructions, tunnel-and-cuff reimplantation of the ureter into the bladder, and Y-V revision of the vesical outlet. This last step should be the usual one, unless there are clear indications to the contrary. With proper selection and adequate treatment, many of these young urinary cripples can acquire a nearly normal functioning excretory system.

OPHTHALMOLOGY

Progress of Metastatic Carcinoma of the Choroid Secondary to Mammary Neoplasm. D. Stenhouse Stewart. Brit. J. Ophth. 44:53-55 (Jan.) 1960 [London].

A 49-year-old woman attended an ophthalmic outpatient department, complaining of sudden deterioration of vision of the left eye 3 days before. Her physician, who suspected retinal detachment, reported that she had undergone a right radical mastectomy 4½ years previously, for stage 2 carcinoma, on account of which she had been under treatment by radiotherapy. The macular area of the left eye appeared gray and slightly elevated. As the diffuse but slight elevation of the macula had the appearance of an inflammatory or serous condition rather than that of a neoplasm, it was decided to defer radical action and to observe the progress. It was felt that, if the swelling represented metastasis from the primary carcinoma, it could hardly be a solitary manifestation, so that immediate removal of the eye would have no lifesaving quality. In the course of 3 months the upper half of the visual field was almost completely lost. The retinal detachment in the macular area was flatter, although more extensive. Some months later malignant skin infiltrations were observed on the neck, chest, and back. More than a year after the woman had first reported visual deterioration, extensive secondary deposits were noted in the pelvic bones. Though doomed by carcinomatous metastasis, the woman had exceeded the "5-year survival period."

Glaucoma Survey of Pittsburgh and Environs. R. J. Gray. Pennsylvania M. J. 63:205-208 (Feb.) 1960 [Harrisburg].

A mass glaucoma screening program, with unified medical sponsorship and a plan for adequate follow-up, was conducted in Allegheny County by the Pittsburgh Ophthalmological Society under the auspices of the Pennsylvania Association for the Blind. Determinations of visual acuity, examinations of the fundus, and measurements of intraocular pressure were made in 20,994 patients. The tonometer foot plates were cleaned with cotton dipped in aqueous benzalkonium (Zephiran) chloride. Tetracaine (Pontocaine) hydrochloride or proparacaine hydrochloride (Ophthaine) was used as a local anesthetic, and no adverse reactions were reported. Of 1,198 patients (499 men and 699 women) suspected of having an elevated tension after an examination utilizing detailed tests, 378 (1.8%) were proved to have glaucoma in one or both eyes; 598 did not have glaucoma, but 319 of them had other ocular defects; 279 had normal eyes; and of the remaining 223 patients, reports were not obtainable. The screening not only detected unknown glaucoma but also provided a means for excellent public education on the need for, and the value of, adequate eye care.

PATHOLOGY

Significance of Cytology in Cancer Diagnosis. O. T. Messelt. Tidsskr. norske laegefor. 80:23-28 (Jan. 1) 1960 (In Norwegian) [Oslo].

The cytological method in the diagnosis of cancer is a method which with high degree of exactness can disclose a cancer or a precancerous condition at a clinically early stage of the disease. Pulmonary cancer can be revealed at a time when roentgenologic diagnosis is still negative. Since the expectorate can be used as smear material, the practitioner has been given a valuable and simple aid toward recognition of pulmonary cancer at an early stage. If it could become the practice to send in smears for examination for cancer at the time that tests are made for culture and bacteriological examination for tuberculosis (instead of waiting for the results of the latter tests), additional valuable time could be saved. With regard to cancer of the cervix, the method can in most cases reveal the cancer at a time when it is not yet macroscopically visible and when there is no clue as to where the biopsy specimen should be taken. Obtaining the smear sample is so simple that it can be done in any physician's office without special equipment, and can be repeated as often as desired without trouble for the patient.

Malignant Peritoneal Mesotheliomas: A Clinicopathological Analysis of 12 Fatal Cases. D. J. Winslow and H. B. Taylor. Cancer 13:127-136 (Jan.-Feb.) 1960 [Philadelphia].

The material for this study consisted of slides, blocks, tissues, and autopsy protocols from the files of the Armed Forces Institute of Pathology. Autopsies with the diagnosis of mesothelioma listed at the institute showed 20 cases in which the peritoneum was exclusively or almost exclusively involved. In 8 the diagnosis was somewhat doubtful; the remaining 12 were selected for study. The clinical course in the 12 patients was one of increasing abdominal discomfort, recurrent ascites, gastrointestinal disturbances, and severe loss of weight. Death was due to the progressive growth of the tumor over large areas of visceral and parietal peritoneum. Superficial invasion of parenchymal organs and metastases to lymph nodes occasionally occurred, but distant parenchymal metastases was not evident in this series. Direct extension through the diaphragm and secondary involvement of the pleura were noted in 3 cases.

The histological pattern of the tumors varied greatly, even in tissue specimens from one autopsy, but tubular, papillary, space lining, and solid types of cellular patterns were most frequent. Epithelial intracytoplasmic carminophilic mucinous material was not found in the tumors, but intracytoplasmic fat and intercellular hyaluronidase-labile substance were demonstrated. In reviewing the literature, the authors found 13 other reports of peritoneal mesotheliomas, which contained striking clinical and pathological resemblance to the cases reported in this paper.

The Sensitization Response in Patients with Cancer of the Uterine Cervix. J. B. Graham and R. M. Graham. Cancer 13:5-14 (Jan.-Feb.) 1960 [Philadelphia].

Cancer disease involves the tumor and the host's reaction to the tumor. Until quite recently little attention has been paid to host resistance, but the authors show that at least one factor in the host can be investigated by the study of the sensitization response. Some patients with cancer of the cervix have basal cells with dense basophilic, finely vacuolated cytoplasm in the vaginal smear before any treatment. These cells come from the parabasal layer of the nonmalignant squamous epithelium of the cervix and vagina. When a fair proportion of the desquamated nonmalignant epithelial cells are of this type, the patient and the cancer usually respond favorably to radiation therapy. Such a patient seems sensitized to the subsequently applied irradiation. The sensitization response (SR) is determined by differentially counting 100 or more consecutive nonmalignant epithelial cells in the vaginal fluid aspirated from the region of the cervix prior to local examination or treatment. The smears are fixed and stained according to the Papanicolaou technique. Superficial, intermediate, and basal cells are counted, but the SR is considered significant only if found in the basal cells. Those patients who have 10% or more SR cells are said to have a marked or good sensitization response. If 9% or less is present, the patient is said to have a poor sensitization response.

The material presented here on primary cancer of the cervix and sensitization response consists of 5 different series totaling 766 cases. The morphologic characteristics of the SR cells and the 5-year salvage rates in patients treated by irradiation or by surgery are discussed. The authors also explain the division of the SR at the 10% level, and report on the incidence of the SR, the reproducibility of the SR counts, and the influence of various factors, such as age and menopause, on the SR.

The sensitization response is a change in the normal cells which presages a favorable response of the tumor to irradiation and an unfavorable result if surgery is applied. It permits rational selection for the mode of treatment. The theoretical implications are intriguing, for here is a normal cell that conditions the clinical behavior of the cancer. It is an epithelial cell whose traditional role has been mechanical envelopment and protection of the body. However, some more subtle form of resistance must be invoked to explain the influence of these cells on cancer. As an index of host resistance, the SR may afford some insight into the manner in which the cancer is healed with the help of radiation.

Factors in Prognosis in Cancer of the Uterine Cervix: Desquamation of Malignant Cells. R. M. Graham and J. B. Graham. Cancer 13:15-19 (Jan.-Feb.) 1960 [Philadelphia].

If 100 patients with stage 1 cancer of the cervix have a radical hysterectomy and regional lymph node dissection, it will be found that the lymph nodes of about 17 have been invaded by cancer. Why does one patient have involved nodes and another not, even though the primary lesion may be of identical size and histological picture? This must represent a difference in the biological behavior of the 2 tumors. The authors felt that a study of the rate of desquamation of malignant cells from the surface of the lesion may contribute to an understanding of this problem. They examined the vaginal smears of 635 patients with cancer of the cervix, making differential counts for the percentage of malignant cells present. It was found that there is great variation in the number of malignant cells present in the pretreatment smear. The lymph node involvement correlated directly with the percentage of malignant cells in 192 cases—the greater the number of such cells in the vaginal smear of a patient, the greater the number of nodes involved. Correlation could also be obtained with 5-year survival—the fewer the malignant cells, the greater the possibility of survival if the treatment were surgical. The reverse was true in the patients treated by radiation. The theoretical implications of these findings are briefly discussed.

Serum Quinine Oxidase Activity in Patients with Liver Disease. H. Baier. German M. Month. 5:15-22 (Jan.) 1960 (In English) [Stuttgart, Germany].

Serial determinations of serum quinine oxidase activity were performed in a series of patients with various types of liver disease. Thirty-seven patients had recently acquired hepatitis. Fourteen patients had obstructive jaundice due to gallstones; 8, obstructive jaundice due to malignancy; 13, cirrhosis; 4, carcinomatous metastases in the liver; 3, cholangitis; 5, secondary involvement of the liver due to other diseases; and 4, congestion of the liver due to heart failure. The serum quinine oxidase level was greatly elevated in cases of hepatitis. The curve of activity showed a distinct peak. The fall in serum quinine oxidase activity coincided with or followed that of the serum bilirubin level. Even minor degrees of parenchymal damage were associated with raised serum quinine oxidase levels. In obstructive jaundice serum quinine oxidase activity was usually either absent or minimal (up to 5 units); when a slight elevation was present, the curve of serial estimations remained flat. Serum quinine oxidase estimation does not differentiate between benign and malignant obstructive jaundice. In other forms of parenchymal liver damage (cirrhosis, congestion, metastases, cholangitis), the serum quinine oxidase activity appeared to be elevated in proportion to the amount of liver damage. Quinine oxidase activity was not demonstrable in the serum of healthy subjects.

Electron Microscopy Studies of Butter and Corn Oil in Jejunal Mucosa. W. A. Thomas and R. M. O'Neal. A. M. A. Arch. Path. 69:121-129 (Feb.) 1960 [Chicago].

The authors devised a dietary method for the production of arterial thrombi and infarcts in rats. Animals fasting for 24 hours were fed a single meal of butter, corn oil, sugar solution, or water by gastric tube, and then sections of the jejunal mucosa were examined by phase and electron microscopy for the presence of absorbed substances. Osmophilic material suggestive of lipids was not observed in the mucosal cells of the fasted rats fed sirup or water; but osmophilic masses were observed in the epithelial cells of the jejunal mucosa in all the rats fed corn oil and killed within 10 to 20 minutes after feeding, and in 1 out of 5 rats fed butter and killed within the same lapse of time after feeding. There were, however, distinguishing characteristics between the morphologic features in the jejunal mucosa of rats fed butter and that of rats fed corn oil. In rats fed corn oil, lipid was observed in the lumen and within the mucosa in the form of rounded, jet-black masses, varying in size; in rats fed butter, lipid was observed in the lumen and within the mucosa in much the same position as in rats fed corn oil, but instead of round forms, irregular linear and crescent forms were usually found. The authors believe that the difference in appearance of butter and corn oil in osmium-fixed tissue is due to the different degrees of saturation of the 2 fats. Further studies are necessary to determine with certainty whether each of these fatty substances has individual identifying characteristics.

RADIOLOGY

Further Observations on Late Radiologic Pictures of Pleuropulmonary and Skeletal Metastasis Due to Cancer of the Breast After Bilateral Oophoroadrenalectomy. E. Bullo and V. C. Catania. Tumori 45:783-800 (Nov.-Dec.) 1959 (In Italian) [Milan, Italy].

A study on the benefit that 51 patients with cancer of the breast, who were observed at the National Cancer Institute of Milan, derived from bilateral oophoroadrenalectomy is reported. The patients presented metastatic involvement of the respiratory apparatus and/or of the skeleton. Metastatic involvement of the respiratory apparatus was observed in 30 patients; 20 patients presented abundant pleural effusions whose neoplastic nature was confirmed on cytomorphologic examination, while 16 presented nodular dissemination in the pulmonary fields or localizations in glands of the hilus with invasion of the pulmonary lymph nodes. Neoplastic involvement of the skeleton was observed in 31 patients; 25 presented involvement of the pelvis, 16 of the vertebral column, and 18 of the ribs. Neoplastic manifestations were mostly of the osteolytic type, rarely of the osteoblastic type or mixed.

Periodic roentgenologic examination showed a rapid and steady absorption of the pleural effusion and a disappearance—not so rapid and less frequent—of the lymphangitic growth, of the hilar adenopathies, and of the metastasis of the lung. Of particular interest were the modifications of the bones in the osteolytic neoplastic foci and in other parts of the skeleton. The authors point out that these modifications should be studied not only periodically but also systematically. Healing of the osteolytic foci occurred in different ways; in some cases it consisted of a gradual reduction or rarefaction of the foci with the formation of a normal trabecular structure, in others in an intensive recalcification with signs of osteosclerosis, and in still others in osteosclerosis which was followed by the formation of a normal bone structure. Roentgenologic examination may show contemporaneously the regression of osteolytic manifestations and the appearance of new pathological foci in the same bone. Particular non-neoplastic changes of the skeleton after diffuse decalcification were observed in some patients some time after surgery. It is believed that these changes are related to conditions of hormonal imbalance.

Retrospective View of Survey Photofluorograms of Persons with Lung Cancer. L. W. Guiss and P. Kuenstler. *Cancer 13:91-95 (Jan.-Feb.) 1960* [Philadelphia].

The controversy regarding the validity of interpretation of minifilms has been intense. The disagreement over the merit of this technique for lung screening caused a representative group of persons interested in this problem to hold conferences. They have agreed on the following points: 1. The minifilm, if properly read, is adequate as a screening tool. 2. There should be a dual reading of all such minifilms. 3. The number of minifilms evaluated by one radiologist at any given session should be limited, so that a fatigue factor would not invalidate the readings. A request has been made for a retrospective study to be carried out on those patients who had minifilms in the 1950 Los Angeles County chest roentgenographic survey and who subsequently died of lung cancer. The intent is (1) to ascertain what the original interpretations were, and (2) to undertake a dual rereading of the original minifilms to check the validity of the interpretations.

Great variation in the interpretation of pulmonary minifilms may occur, depending on the bias of the individual reader and intentional policies of "underreading" or "overreading." These inherent differences may be significantly exaggerated by reader fatigue, error, and omission of second reviews. Dual reading of the "negative" films in this study would have resulted in definite "abnormal" reports in one-fourth of them and "questionably abnormal" reports in a like number, thereby greatly increasing the number of suspects. Dual reading of the "positive" films in this same study would only have confirmed the presence of disease.

Retrospective review of the photofluorograms of patients who were to die of lung cancer within 5 years has revealed gross underreading and suggests that much potential salvage of lung cancer patients was lost through either inadvertent or intentional underreporting. Some attempt should be made to develop a more accurate method of reading minifilms and thus avoid the extreme variability and inexactness inherent in the present system. If chest roentgenograms are to be used efficiently for detecting lung cancer or any other pulmonary disease, scientific criteria must be developed and applied to this procedure.

Betatron Treatment of Inoperable Bronchial Cancer. E. Poppe. Tidsskr. norske laegefor. 79:1452-1455 (Dec. 15) 1959 (In Norwegian) [Oslo].

Only a small number of persons with bronchial cancer can be treated by radical surgery. Thus, there is always need for palliative treatment, both for the patients with inoperable primary bronchial cancer and for those with recurrence after earlier radical operation. In the Norwegian Radium Hospital treatment of inoperable bronchial cancer with ultrahard short roentgen rays from a 31-mev betatron has been found to give excellent palliative effect. Because of the favorable deep apportionment and smaller spread to the sides, betatron treatment can be carried out with less trouble and strain for the patient than the conventional roentgen irradiation previously applied.

Further Studies on the Accuracy of Oral Cholecystography. H. L. Baker and J. R. Hodgson. Radiology 74:239-245 (Feb.) 1960 [Syracuse, N. Y.].

The degree of accuracy of cholecystographic diagnoses made in the year 1957 at the Mayo Clinic was studied by correlating the operative and pathological findings of 1,207 surgically treated patients with the roentgenologic diagnoses. The results of this study in which iopanoic acid was used as the radiopaque medium were compared with 2 previous series in which iodoalphionic acid and iophenoxic acid were employed. The investigation revealed that 1.9% of the 1,207 diagnoses were in error. The use of iopanoic acid did not materially increase the percentage of gallbladders that exhibited some degree of function. There was, however, a definite increase in the number of gallbladders with marked concentrations of the medium. There was no evidence that the increased opacity of iopanoic acid obscured tiny calculi or rendered normally visible abnormal gallbladders which did not contain stones. The diagnosis of normally functioning gallbladder was found to be correct in 98.3% of such cases. This represented an improvement over the authors' previous series and was attributable to improvement in both roentgenographic technique and interpretation. All gallbladders called poorly functioning were found to be diseased. The increased accuracy of this diagnosis seemed to have a direct relationship to the medium employed. Stones were found in 98.0% of the cases diagnosed preoperatively as cholelithiasis. This is a decrease in accuracy from a previous series and resulted from misinterpretation of data made available as a result of the increased opacity of the medium. Polyps, papillomas, or adenomas were found in all cases in which they were reported. No change was observed in the incidence of "normal gallbladders" among the nonfunctioning group; 97.8% of these organs were found to be diseased.

PUBLIC HEALTH

Etiology of the 1927-28 Epidemic of Dengue in Greece. M. Theiler, J. Casals, and C. Moutousses. Proc. Soc. Exper. Biol. & Med. 103:244-246 (Jan.) 1960 [Utica, N. Y.].

In 1927-1928 an extensive epidemic of a disease diagnosed as dengue occurred in Greece. The total number of cases probably exceeded one million. The diagnosis of dengue was made entirely on clinical grounds. During recent years several viral agents have been isolated in mice from patients diagnosed as having dengue. Two of these are known as type 1 and type 2 of dengue virus. These types are distinct from each other, although there is a marked immunological overlap. Investigators in Israel have shown that infections in man with the West Nile virus may produce a disease which clinically resembles dengue. The 2 types of dengue virus and the West Nile virus belong to Casals' group B of immunologically related arthropod-borne viruses. Serologic investigations were made on serums obtained from residents of Athens to determine, if possible, the etiology of the dengue epidemic in 1927-1928.

Serum specimens were obtained in 1958 from 56 Athenian residents. On the basis of age of these residents, the specimens could be divided into 2 groups: 27 were from persons, aged 32 years or older, who were living at the time of the 1927-1928 epidemic, and 29 were from persons who, since they were 29 years of age or less, had been born subsequent to the epidemic. To determine the presence or absence of antibodies, emphasis was placed on hemagglutination-inhibition (HI) tests. All serums were tested against 7 different group B virus antigens: West Nile (strain IG 2266); dengue, types 1 and 2; Japanese encephalitis; yellow fever (Asibi); Russian spring-summer encephalitis (RSSE); and SA H 336. The last named virus is an agent closely related to Uganda S.

These studies provided an opportunity for acquiring information about the persistence of HI antibodies after a group B arthropod-borne virus infection. Evidence was obtained that the epidemic of 1927-1928 was in all probability due to dengue virus, type 1, because corresponding antibodies were demonstrated in about 70% of serums from persons living at the time of the epidemic, whereas serums from persons born after the epidemic were all free from such antibodies. In most regions where the group B arthropod-borne viruses occur, infections with these viruses are endemic, and persons are exposed to repeated infections by one or more group B agents. In the present instance, however, the complete absence of any group B antibodies in the serums of the younger age group shows that no group B arthropod-borne virus infection has occurred in Athens since the epidemic of 1927-1928. Under these circumstances, the close correspondence between the results obtained in the HI and neutralization tests is good evidence that HI antibodies persist for at least 30 years after an infection with dengue virus, type 1.

Research on the Epidemic of Typhoid and Paratyphoid in Trieste. G. Rottini. Minerva med. 51:102-105 (Jan. 13) 1960 (In Italian) [Turin, Italy].

A total of 16,006 cases of typhoid or paratyphoid were recorded in Trieste, Italy, and the surrounding area during the period from 1920 to 1948. Only 5 cases of paratyphoid, type A, were observed. The morbidity rate for typhoid was 20 per 1,000 at the beginning of the 29-year period studied and 2 per 1,000 at the end. The morbidity rate for paratyphoid declined from 4 or 5 per 1,000 in 1920 to about 0.5 per 1,000 in 1948. This decline was progressive throughout the entire period studied, with the exception of the years 1941-1945 when the morbidity rate for typhoid reached a high of 54 per 1,000 per year, and that for paratyphoid a high of 7 per 1,000 per year. The highest frequency for both types of infection was recorded during the months of August to October. The highest morbidity rate was observed among patients 10 to 30 years of age. The author points out that during the 30-year period the frequency of morbidity tended to shift toward early infancy and, proportionally more so, toward the age groups over 50.

The total mortality rate for typhoid oscillated irregularly between 5 and 10% until 1948, when it declined spontaneously; the decline became more marked after 1951 when chloramphenicol became available for treatment. A similar behavior has been recorded for the total mortality rate for paratyphoid, which oscillated between 5 and 2.5% until chloramphenicol came into use. Before the adoption of the antibiotic the highest mortality rate for both types of infection was recorded among sucklings. The prognosis was more favorable, especially in the case of paratyphoid, among children 1 to 5 years of age. Total mortality rates were 2.1% for typhoid and 0.70% for paratyphoid among children 6 to 10 years of age, and 7.3% for typhoid and 1.2% for paratyphoid among patients over 10 years of age. After the adoption of chloramphenicol, the total mortality rate for both types of infection was nonexistent among nursing infants and among children 6 to 10 years of age. A 60% decline was observed in the mortality rate among children 1 to 5 years of age, and an 87.7% decline among those over 10 years of age.

QUESTIONS AND ANSWERS

HYPERPARATHYROIDISM

To the Editor:—*What are the best laboratory procedures for making a diagnosis of hyperparathyroidism in a person who has severe renal insufficiency? No bone changes have been observed—the phosphorus level is elevated, serum calcium and alkaline phosphatase levels are normal, and the blood urea nitrogen level is 64 mg.%. The patient has bilateral renal calcification.*

James E. Cimino, M.D., Orlando, Fla.

Answer.—In renal failure with phosphorus retention "secondary" hyperparathyroidism is usually present and the situation is chemically nearly identical to that of primary hyperparathyroidism with supervening renal failure. In some of the latter cases the blood calcium level fails to fall as low as is usually seen in uremia of other origins and may be considered relatively high, that is, high for the severity of the degree of uremia. If the phosphorus level can be lowered by forcing fluids, administration of massive doses of aluminum hydroxide, or dialysis, the calcium level may become clearly high. It is worthwhile to attempt to establish the diagnosis, since fairly severe renal insufficiency may improve when a causative parathyroid adenoma is removed.

The nature of the kidney calcification and a careful history are more apt to establish the diagnosis than is the blood chemistry. If any stone previously passed or removed is available it should be analyzed. Diffuse nephrocalcinosis suggests hyperparathyroidism, renal tubular acidosis, vitamin D intoxication, or milk alkali syndrome. Oxalate stone is common in hyperparathyroidism. Large, layered phosphate stones suggest that urinary tract infection was an early if not the primary event.

Taking of the medical history should include inquiry about urinary tract infection and instrumentation; intake of alkali, vitamin D, or excessive intake of milk; and other causes of stone. Finally, the ability of multiple small cystine stones to imitate the roentgenographic picture of nephrocalcinosis should not be forgotten.

A STATISTICAL COHORT

To the Editor:—*During the past year I have seen increasing references to cohort and cohort rate in articles dealing with biometry. What is the definition of these terms?*

M.D., California.

Answer.—A cohort is a group of persons starting life (or, in some instances, marriage) during the same year or other time interval. Thus the birth cohort of 1900 consists of persons born in that year and the marriage cohort of 1930-1934 consists of persons married during those years. A cohort rate is a measure of the experience, for example of mortality or fertility, of a cohort as it goes through life. Cohort rate is in contrast to a period rate, which is a measure of the experience of an entire population during a period of time.

PREGNANCY AND JET AIRPLANE TRAVEL

To the Editor:—*A newspaper printed a report that an obstetrician advised an actress not to fly in jet airplanes until after termination of her pregnancy but said that flights in ordinary planes are all right. What is the basis for this recommendation?*

George R. Mason, M.D., Moultrie, Ga.

Answer.—The following statement will be published in a booklet which will be sent to all physicians by a special committee of the Aerospace Medical Association: "Physicians generally agree that a woman with an uncomplicated pregnancy is not sick, that she is a normal individual undergoing a normal physiological process. Most airlines feel that the only contra-indication to air transport of the pregnant woman is the danger of precipitate delivery during flight. All airlines accept the pregnant woman during the seventh month of gestation and the majority will transport those in the eighth month. In order to be accepted for air transport during the ninth month, the pregnant woman must present a certificate signed by her physician certifying that he has examined her within 72 hours of departure, has found her to be physically fit for transportation, and states the estimated date of birth. The following is a policy recommended by the Airline Medical Directors Association: Any woman in pregnant condition shall be accepted from the beginning of the first month on through the end of the eighth month of gestation without question. Any woman in the ninth or last month of pregnancy shall be accepted who can furnish a certificate from an obstetrician dated within 72 hours of departure, stating that he has examined and found her to be physically fit for transportation from (place) to (place) on (date) and the estimated time of birth for the baby as (date)."

Pregnant travelers should select rearward facing seats, if possible, to allow use of a loosely fastened seat belt across the thighs under the fetal bulge. It is not unusual for those near term to develop false labor pains within a day or so after flight and any patient traveling in the latest stages of pregnancy

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The answers here published have been prepared by competent authorities. They do not, however, represent the opinions of any medical or other organization unless specifically so stated in the reply. Anonymous communications cannot be answered. Every letter must contain the writer's name and address, but these will be omitted on request.

should be forewarned that this might occur. A study of abortion in 1,000 women aged 16 to 42 years, traveling by air during World War II, revealed no correlation between abortion and flying. Air travel is not harmful to a normal pregnancy regardless of the duration of the pregnancy. There are no reliable reports of deleterious effects to the unborn child or mother, due to premature labor, or hypoxia, in the altitudes traveled by commercial aircraft.

The medical committee of the Air Transport Association of America, which comprises the medical directors of the six major airlines, has adopted the recommendation of the airline medical directors as quoted above as far as domestic travel is concerned. To date there is no record of a full-term viable birth occurring on any domestic scheduled airliner in the United States, with the exception of several on the Puerto Rican run.

The policy for overseas passengers is to advise them not to fly after the eighth month of pregnancy. This policy is predicated on travel time. With the advent of jet aircraft, the present policy for domestic travel may be extended to overseas travel because of the shorter duration of flights on the jet planes. There appears to be no explanation for the recommendation, referred to in the inquiry, that women in the later stages of pregnancy should avoid travel in jet aircraft. The jet aircraft has a much shorter travel time, is pressurized at greater levels, and therefore is much more adapted to the human physiology than some of the conventional aircraft. Possibly the obstetrician had not been fully informed of the physiological and practical facts regarding air travel in jets. It is indeed unfortunate that this recommendation received such wide dissemination.

ATYPICAL MYCOBACTERIAL INFECTION

To the Editor:—*Please discuss the communicability of atypical pulmonary tuberculosis. A patient with this disease was recently discharged from a sanitarium. He is an elderly man who plans to live alone in an apartment and do his own cooking.*

M.D., Georgia.

Answer.—It is incorrect to describe an infection due to atypical mycobacteria as atypical pulmonary tuberculosis, since these mycobacteria can be distinguished from the human tubercle bacillus. There is no proof to date that the various atypical mycobacteria are transmissible from one human being to another. All the unclassified or atypical mycobacteria have been found in the sputum of normal persons. These organisms are classified by Runyon into groups 1, 2, 3, and 4. Group 3, the nonphotochromogen, is the type most frequently encountered in the southeastern part of the United States. This type accounts for 1 to 2% of patients with chronic pulmonary infections admitted to tuberculosis hospitals in this area. There is, as yet, no report of such infections occurring in the same family, and cross-infection with atypical mycobacteria in hospitalized patients has not occurred. Patients with atypical mycobacterial infections can acquire tuberculosis in tuberculosis hospitals, unless they are isolated. Results of skin tests made with use of purified protein derivative prepared from the nonphotochromogens indicate that infection is common in the southeastern United States. Clinical disease due to these mycobacteria is relatively uncommon and is frequently associated with other chronic lung disease, such as pulmonary emphysema and tuberculosis.

Prolonged hospitalization is of little benefit to the older patient who is not a candidate for resectional surgery. Medical treatment is of limited value, since these organisms are resistant to most antimicrobial agents. Resectional surgery in the appropriate case is the most effective form of treatment. The elderly patient in question is an ideal candidate for discharge, since, after a short period, such persons have received maximum hospital benefit.

STAPES MOBILIZATION AND DEAFNESS

To the Editor:—*Please give an outline of the stapes mobilization operation which is performed for deafness. Is it usually successful? Where can one have it performed?*

Jean Jongewaard, M.D., Jefferson, Iowa.

Answer.—The stapes mobilization procedure and its more recent refinements represent a notable advance in the surgery of otosclerosis. These procedures are less arduous for the patient than the fenestration operation, largely because the period of hospitalization is short and there is no mastoid or fenestration cavity to heal over. The range of types of otosclerotic deafness which can be treated by mobilization is wider than the range suitable for fenestration. For example, a patient with bilateral otosclerosis who has only a mild hearing loss can be treated by stapes mobilization, whereas fenestration would be contraindicated. The fenestration operation is successful in a greater percentage of patients than is the stapes mobilization procedure, but when mobilization is successful, the hearing results are often much better than those afforded by fenestration. A disadvantage of stapes mobilization is that, while gaining immediate and worthwhile improvement in hearing, a significant number of patients gradually revert to their preoperative hearing level because the stapes footplate has again become fixed. If mobilization is carried out and fails immediately or later, fenestration is still possible; the reverse is not true.

Operative technique involving the stapes has recently been modified so that now, when simple manipulation fails to free a fixed stapes, the stapes may be removed in part or completely and a graft and prosthesis put in its place. Results from this more complex procedure are an advance over the original mobilization technique in terms of the degree of hearing improvement obtained and of the permanence of this improvement.

A patient's advanced age is not a contraindication to either of these stapes procedures. It is possible, however, that with advancing age a marked high-tone nerve deafness may develop which could militate against the chances of a successful hearing result. A thorough audiometric analysis should be made to determine the suitability or unsuitability for surgery.

There are a number of places in the United States where both types of stapes operations are performed. In general, all schools of medicine of good repute have on their staffs otologists thoroughly experienced in all of the stapes mobilization and graft procedures.

DISINFECTION OF WRESTLING MATS

To the Editor:—*The members and coach of a high school wrestling team have been afflicted with infections in skin abrasions sustained from contact with wrestling mats. Can you suggest an effective way of disinfecting these mats?*

Frank R. Peterson, M.D., Butte, Mont.

Answer.—There is no easy solution to this problem, because the covering of the mat presumably is made of canvas and thus is permeable to secretions containing bacteria. Disinfection by the ethylene oxide-gas method is recommended, since heat sterilization of such a large object is impracticable. The gas penetrates readily and causes no damage to textile materials. The mat should be rolled and tightly sealed in a covering of plastic sheeting. Ethylene-oxide gas is then forced into the plastic bag, which is kept hermetically sealed for 24 hours. Since ethylene oxide is flammable, it is usually dispensed in a 10% mixture with 90% carbon dioxide or hydrogenated hydrocarbons containing fluorine atoms. An easier method would be to remove the mat from use for two weeks and expose it to fresh air and sunlight. The surface of the mat should, during the two-week period, be scrubbed several times with one of the many detergents available. This method would not accomplish complete sterilization but would kill most of the bacteria. Canvas-covered mats subject to repeated body contacts should be protected by a heavy plastic material which can be removed each day for cleansing. The source of bacteria in the infections described is usually a wrestler with infected lesions. Hence, the most important measure in the ultimate control of such infections would be a daily surveillance of and elimination from participation of the wrestlers with lesions until they have recovered.

DIABETES AND PREGNANCY

To the Editor:—*What is the most effective medical management of a patient who has a family history of diabetes? The patient is not obese and has never had glycosuria, but the result of her glucose tolerance test indicates a marginal diabetic condition. She has had recurrent episodes of monilial vulvovaginitis. Of four pregnancies, three ended as spontaneous abortions and one continued to term with delivery of a living, healthy 4-lb. 4-oz. infant. She wishes to have another baby.*

J. Bothwell Traylor, M.D., Athens, Ga.

Answer.—Treatment of a patient with a family history of diabetes and a glucose tolerance test result indicating mild diabetes consists in correct dietary control of food intake. This can be accomplished by determining the blood sugar level one hour after the patient eats breakfast; the blood sugar level should not exceed 150 mg.% (Folin-Wu). If it is abnormally elevated, the carbohydrate content of the diet should be decreased to 100 to 130 Gm. per day, with maintenance of normal weight by an increase of dietary protein and fat. If the blood sugar level is not reduced to normal thereby, sulfonylureas (tolbutamide or chlorpropamide) may be used in small doses. While the incidence of abortions has not been shown to increase in diabetic women—unless acidosis occurs during the pregnancy—diabetes can progress in severity, and a mild diabetes can become overt during pregnancy. Hence, the necessity for close observation of a diabetic state during pregnancy will be of therapeutic benefit to the patient and of value in obstetric care.

PROLONGED LACTATION AFTER MISCARRIAGE

To the Editor:—*A 35-year-old woman who has not yet carried a pregnancy to term has had five miscarriages. She has had profuse milky discharge from both breasts since her last miscarriage five years ago. Her condition has been studied and she has received synthetic estrogens and testosterone in attempts to stop the discharge, without improvement. Her breasts are engorged and the discharge, on analysis, was reported to be similar to normal breast milk. What can be done to control this condition?*

E. S. Sarvis, M.D., Naalehu, Hawaii

Answer.—This question poses two problems: repeated abortion and persistent lactation after the last abortion. The question, as stated, gives no information on either the duration of each of the lost pregnancies or the results of laboratory tests which might provide a clue to the causal factors involved. Similarly, is the persistent lactation accompanied by amenorrhea? If so, one is probably dealing with the rare Chiari-Frommel syndrome in which amenorrhea and lactation continue for some years after a pregnancy. Arginz and Del Castillo believe that it is due to an "eosinophilic hyperfunction of the anterior lobe of the pituitary with increased production of prolactin." Another possible cause of this syndrome is a pituitary tumor.

In general, treatment is most unsatisfactory. Temporary improvement may be achieved by administration of estrogen-progesterone or estrogen-androgen preparations. If a space-taking pituitary lesion is present, x-ray therapy or operation may be indicated.

AURICULAR FIBRILLATION AND MITRAL COMMISSUROTOMY

To THE EDITOR:—*Should an attempt be made to convert auricular fibrillation to a normal rhythm in patients who have had a mitral commissurotomy performed? Many of these patients had fibrillating hearts before the procedure which continue fibrillating postoperatively. What is the experience of physicians who have followed the progress of such patients over the years?*

M.D., Washington.

ANSWER.—The problem of attempting to convert atrial fibrillation to normal rhythm after operation for mitral stenosis is not entirely settled. If a patient is in normal sinus rhythm at the time of operation, or within a short period before operation, it makes sense to convert a postoperative arrythmia promptly and this is usually easy to do. If the patient has been fibrillating for a long time, is in the older age group, and has a well-controlled heart rate with good myocardial reserve, fibrillation is usually accepted as a satisfactory clinical state and conversion is not attempted. If the patient's fibrillation is of relatively short standing, if there are no intracardial clots, and if the heart appears healthy, an effort is usually made to convert the patient to normal rhythm, either electrically during the course of operation or postoperatively with quinidine sulfate therapy. In both cases, the conversion has rarely been permanently successful.

GLAUCOMA AND HYPOTHYROIDISM

To THE EDITOR:—*Two women, aged 45 and 52 years, respectively, have glaucoma associated with hypothyroidism. I have been unable to find any reference to a cause-and-effect relationship between these two diseases. Is there any established connection of the two or any rational explanation of a myxedematous state producing increased intraocular tension?*

M.D., Pennsylvania.

ANSWER.—Glaucoma is not usually associated with hypothyroidism. The incidence of glaucoma in the age group given is about 2 to 3%. Since hypothyroidism is predominantly a disease of women during the menopause, it is not surprising that the two conditions frequently coexist. Conversely, glaucoma is frequently associated with the exophthalmos of hyperthyroidism. It is felt that, in the latter state, it is the compression of the venous outflow channels by the increased orbital contents that produces an increased intraocular pressure. The myxedema of hypothyroidism apparently does not involve the retrobulbar tissues.

SIDE-EFFECTS OF SUGAR SUBSTITUTES

To THE EDITOR:—*Assuming that there is no question of either diabetes or of a condition in which sodium intake is important, can the indiscriminate ingestion of saccharin or cyclamate sodium or calcium to reduce or prevent obesity be harmful to dieting laymen?*

Donald Macomber, M.D., Brunswick, Maine.

ANSWER.—There is no evidence that the continued use of either saccharin or cyclamate sodium has any harmful effects.

The food protection committee of the National Research Council has published a pamphlet entitled "The Safety of Artificial Sweeteners for Use in Foods." This discusses thoroughly the acute and chronic toxicity of both cyclamate and saccharin. The conclusion states that the unrestricted use of cyclamate in foods and beverages may result in the formation of soft stools, but that it probably does not interfere with other functions of the intestine and is no health hazard. It is further stated that the maximum amount of saccharin likely to be ingested is not hazardous and that there appears to be no adverse synergistic effect from combinations of cyclamate sodium and saccharin.

PROTHROMBIN TIME DETERMINATION

To THE EDITOR:—*It is frequently stated, "Do not use anticoagulants unless you are certain of your laboratory's ability to perform accurate prothrombin time determinations." At which points in the procedure are errors apt to be made and how can they be eliminated?*

F. M. Furr, M.D., Cuba City, Wis.

ANSWER.—Detailed delineation of estimation of plasma prothrombin by the one-stage method (Quick) and general consideration of objectives, underlying principles, equipment and procedure, and sources of error and limitations are given in chapter 7 of "Coagulation of Blood: Methods of Study" (edited by Tocantins and prepared under the auspices of the National Research Council, New York, Grune & Stratton, Inc., 1955).

WASHINGTON NEWS

Delay Recommended on Aged Health Bills . .
Group Proposes Large Research Effort . .
Welch Blames Politics . .
States Queried on Federal Role . .

POSTPONE ACTION ON HEALTH PLANS, A. M. A. URGES

Members of the House Ways and Means Committee were urged by the American Medical Association to avoid hasty action "in an atmosphere of panic," and put off until next year consideration of plans for health care of the aged.

In a letter sent to all Committee members, A. M. A. President Dr. Louis M. Orr declared: "It has become increasingly apparent that the creation of a sound program requires additional objective appraisal and discussion.

"Clearly, any legislation adopted in haste—during the inevitable tensions of an election year—is likely to harm the very people whom it is intended to help.

"For this reason, we are convinced that further study of the matter is in the best interests of the nation's older citizens and is in the best interests of all citizens, regardless of age.

"As we all know, this is a complex matter, intimately affecting the lives of millions of our citizens. Moreover, many of the facts essential to effective planning are not yet available. They must be obtained in the months remaining before the White House Conference on Aging in January, 1961.

"Obviously, some proponents of compulsory national health insurance have sought to create an atmosphere of panic, in which far-reaching legislation could be rushed through without adequate consideration of the best interests of our aged citizens. This atmosphere had made it difficult, if not impossible, to weigh fully the potential impact of the various legislative proposals that have been offered. In fact, recent proposals have received no hearings whatsoever.

"In our opinion, it would be a tragic mistake for our nation to undertake a vast program, ultimately costing billions of dollars and entering a new and uncharted field, without offering all interested and responsible parties an opportunity to present their viewpoints.

"Consequently, we reiterate our conviction that the only practical and realistic course is to postpone action at this time."

With Congress gearing for adjournment by July 1, time became an important factor in the controversial debate over financing health care for the aged. The House Ways and Means Committee, as of this writing, had not approved any measure in the field, and the future course of legislation involving health care for the elderly hinged to a great extent on what action the committee took.

This is because all legislation involving such taxes as those paid for social security must be originated in the House rather than the Senate, and the Ways and Means Committee is the group that considers tax measures first.

A series of test votes on the issue revealed that there was no overwhelming sentiment on the committee for any of the three approaches before it. The lawmakers, in fact, rejected the Forand bill to finance health care through the social security system, turned down the administration's plan involving the present federal-state public assistance programs, and defeated a proposal to postpone all consideration until next fall. By a single vote, the Committee did direct the staff to prepare a bill that would be a trimmed-down version of the administration plan, but Committee members agreed this was not a valid test of Committee sentiment on the issue.

Noting the lack of time and the confused legislative situation, J. F. Follmann Jr., information and research director of the Health Insurance Association of America, declared the association "believes the question of health care financing for older people deserves the judicious, unhurried appraisal of Congress, because the subject has long-range implication of importance to the economic and social structure of the nation."

Organized labor leaders, meanwhile, stepped up their campaign to win enactment of the Forand bill. They called a rally in Madison Square Garden, New York City, at which proponents of government medicine measures attacked the administration, the American Medical Association, and other foes of compulsory medical schemes.

On the other hand, Arthur S. Flemming, Secretary of Health, Education, and Welfare, and Dr. Thomas S. Parran, U. S. surgeon general from 1936 to 1948, criticized the Forand measure in addresses before the 10th annual Group Health Institute.

The Forand bill "would include a great many persons who are not a part of the problem . . . and it would exclude approximately 4 million of the 16 million persons 65 and over from the program because they are not eligible for social security," Flemming said. In addition, it would impose a compulsory increase in social security taxes on employers and employees alike, he noted.

Dr. Parran said the bill was drafted by persons who are "panning for political gold rather than attempting to meet this very real and serious problem in the best possible way."

ADVISORY GROUP RECOMMENDS VAST RESEARCH OUTLAYS

A congressional advisory group proposed a 264-million-dollar increase in federal medical research expenditures this year "to support a determined attack on the dread diseases."

The present level of support—400 million dollars —"is far from adequate to permit the great advances essential for the future," the group declared in a report prepared for the Senate Appropriations Committee.

The advisory group was headed by Dr. Boisfeuillet Jones, vice-president and administrator of health services, Emory University, Atlanta. Of the 12 committee members, 9 were medical scientists, 3 were informed laymen, and one was a physician with medical administrative experience.

According to the report, "inadequate" federal medical research funds during the last 15 years "have been spent with remarkable efficiency and consistently high standards." By the year 1970, the committee said, such spending could be stepped up to 2 billion dollars a year.

The National Institutes of Health "could effectively use $576,500,000 for orderly growth and development of its present program this fiscal year, and another $87,500,000 in seven new areas justifying special emphasis." These included "a needed appropriation of 55 million dollars to start setting up regional clinical research centers . . . a 12-million-dollar fund for primate research centers and for development of facilities for the production of additional laboratory animals . . . 10 million dollars for the support of international medical research and considerably more for the same purpose in the year to come . . ."

The committee also proposed construction of an international medical facility at NIH, a 5-million-dollar appropriation for the support of instrumentation research, 60 million dollars for building medical colleges, and 50 million dollars for construction of health research facilities.

The administration this year recommended 400 million dollars for medical research—the amount Congress appropriated last year. The House this year voted 455 million dollars, and the measure went to the Senate which in recent years has approved more money than the House for such purposes.

The advisory committee disagreed with assertions by President Eisenhower and others that too much federal spending on research could lower the quality, divert needed medical and scientific personnel from vital work, and stifle private research efforts. "Physicians and dentists constitute less than half of the professional personnel engaged in research," said the group. "Since the number of Ph.D. graduates is increasing rapidly, and the number of supporting personnel is almost limitless, and since modern equipment and techniques have enormously magnified the productivity of the individual investigator, the present relative shortage of physicians and dentists is not a limiting factor on the expansion of our research effort."

Members of the committee, in addition to Dr. Jones, were Alfred Blalock, M.D., Chairman, Department of Surgery, Johns Hopkins University Medical School; Virginia G. S. Burnham, vice-president, Connecticut Manufacturing Co., Inc., Waterbury, Conn.; Michael E. De Bakey, M.D., Chairman, Department of Surgery, Baylor University College of Medicine; Edward Dempsey, Ph.D., Dean, Washington University School of Medicine; Sidney Farber, M.D., Professor of Pathology, Harvard Medical School; Harry Lyons, D.D.S., Dean, School of Dentistry, Medical College of Virginia; Leo Rigler, M.D., Visiting Professor of Radiology, University of California Medical School at Los Angeles; Brig. Gen. David Sarnoff, U. S. Army Reserve, Chairman of the Board, Radio Corporation of America; Cornelius H. Traeger, M.D., Professor of Clinical Medicine, Cornell University Medical School; J. Walter Wilson, Ph.D., Chairman, Department of Biology, Brown University; and Cecil Wittson, M.D., Chairman, Department of Neurology and Psychiatry, University of Nebraska School of Medicine.

ANTIBIOTICS CHIEF RESIGNS

Henry Welch, Ph.D., chief of the Food and Drug Administration's division of antibiotics, resigned at the request of Arthur S. Flemming, Secretary of Health, Education, and Welfare.

In his letter of resignation, Dr. Welch blamed politics for the controversy over his outside income. He called for a "nonpolitical evaluation" of his editorship of two antibiotics magazines—the *Journal of Antibiotics and Chemotherapy*, and *Antibiotic Medicine and Clinical Therapy*.

After staff investigators of the Senate antitrust subcommittee studying the drug industry reported that Dr. Welch had received $287,142 in outside income since 1953, HEW Secretary Flemming demanded his resignation.

"I challenge anyone to search the journals and come up with any article, paragraph or sentence which reflects a lack of editorial or scientific integrity," Dr. Welch said in his letter. He said the columns of his periodicals had been open to full representation of both sides of controversial subjects, and "I reserved the right to review any advertising copy to curb any tendency toward improper claims."

STATES ASKED FOR VIEWS ON FEDERAL AGED ROLE

How far the federal government should go in assisting the states to care for needy older persons was the main question asked of the 50 state conferences now preparing for the White House Conference on Aging in January.

In a pamphlet sent to all 50 state groups, the National Advisory Committee of the White House Conference asked the states to make recommendations on the federal government's role in the field.

The document noted there was "some disposition" in Congress to "explore further the question of federal responsibility." In addition, there are Congressional forces desiring "a broader commitment than exists now on the part of the federal government in the aging field," with large appropriations needed to carry out some of the proposals.

"What are the wishes of the states themselves?" the pamphlet asks. "Do they want federal grants-in-aid specifically keyed to the aging, and are they prepared to provide matching funds should these be required? If so, through what channels would the states then prefer to receive the federal grants?"

The 2,800 delegates attending the conference will meet in 10 major work groups to prepare recommendations. They will cover 20 broad subjects such as housing, recreation, retirement, finances, and health care.

HOW WOULD YOU DEFINE *the ideal diuretic?*

The qualities to be sought in an ideal diuretic have been listed[1] as follows:

"(1) Sustained rather than abrupt violent action.

(2) Reduced capacity for electrolyte upheaval.

(3) Convenience of administration; self-administration (oral, rectal, or subcutaneous).

(4) Decreased toxicity (systemic and local irritant action, especially of the gastrointestinal tract).

(5) Effectiveness where others are ineffectual or contraindicated.

(6) Applicability in cases with a history of allergic reaction to other diuretics."

It would be rash to term any drug ideal. It is safe to say, however, that Aldactone very closely approximates these six requirements. Most importantly, Aldactone often relieves edema and ascites resistant or not optimally responsive to conventional diuretics. By blocking the *action* of the potent salt-retaining hormone, aldosterone, Aldactone, used alone or in synergistic combination with other potent agents, establishes satisfactory diuresis in most edematous patients who have heretofore been considered beyond the help of medical management. Aldactone offers a fundamentally new approach to the control of edema in such disorders as congestive heart failure, hepatic cirrhosis, the nephrotic syndrome and idiopathic edema.

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1. Modell, W.: Am. J. Cardiol. *3*:139 (Feb.) 1959.

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MEETINGS

AMERICAN MEDICAL ASSOCIATION: Dr. F. J. L. Blasingame, 535 North Dearborn St., Chicago 10, Executive Vice-President.

1960 Annual Meeting, Miami Beach, Fla., June 13-17.
1960 Clinical Meeting, Washington, D. C., Nov. 28-Dec. 1.
1961 Annual Meeting, New York City, June 26-30.
1961 Clinical Meeting, Denver, Nov. 27-30.
1962 Annual Meeting, Chicago, June 11-15.
1962 Clinical Meeting, Los Angeles, Nov. 26-29.

AMERICAN

1960

June

American Academy of Tuberculosis Physicians, Miami Beach, Fla., June 11. Dr. George P. Bailey, P. O. Box 7011, Denver 6, Secretary.

American Association of Neuropathologists, Statler-Hilton Hotel, Boston, June 11-12. Dr. Leon Roizin, 722 W. 168th St., New York 32, Secretary-Treasurer.

American College of Angiology, Roney Plaza Hotel, Miami Beach, Fla., June 10-12. Alfred Halpern, Ph.D., 11 Hampton Court, Great Neck, N. Y., Executive Secretary.

American College of Chest Physicians, Miami Beach, Fla., June 8-12. Mr. Murray Kornfeld, 112 E. Chestnut St., Chicago 11, Executive Director.

American Diabetes Association, Inc., Hotel Deauville, Miami Beach, Fla., June 11-12. Mr. J. Richard Connelly, 1 E. 45th St., New York 17, Executive Director.

American Electroencephalographic Society, Belmont Hotel, Cape Cod, Mass., June 10-12. Dr. George A. Ulett, 1420 Grattan St., St. Louis 4, Secretary.

American Geriatrics Society, Americana Hotel, Miami Beach, Fla., June 9-10. Dr. Richard J. Kraemer, 2907 Post Road, Warwick, R. I., Secretary.

American Medical Women's Association, Hotel Carillon, Miami Beach, Fla., June 9-12. Mrs. Lillian T. Majally, 1790 Broadway, New York 19, Executive Secretary.

American Neurological Association, Hotel Statler, Boston, June 13-15. Dr. Melvin D. Yahr, 710 W. 168th St., New York 32, Secretary.

American Physical Therapy Association, Penn-Sheraton Hotel, Pittsburgh, June 26-July 2. Miss Lucy Blair, 1790 Broadway, New York 19, Acting Executive Director.

American Physicians Art Association, Miami, June. Dr. Kurt F. Falkson, 7. E. 78th St., New York 21, Secretary.

American Rheumatism Association, Hotel Diplomat, Hollywood-by-the-Sea, Fla., June, Mr. Gerard W. Speyer, 10 Columbus Circle, New York City, Executive Secretary.

American Society of X-Ray Technicians, Netherland Hilton Hotel, Cincinnati, June 11-16. Genevieve J. Eilert, R.T., 16 Fourteenth St., Fond du Lac, Wis., Executive Secretary.

American Therapeutic Society, Barcelona Hotel, Miami Beach, Fla., June 9-12. Dr. Oscar B. Hunter Jr., 915 19th St., N. W., Washington 6, D. C., Secretary.

Association for Research in Ophthalmology, Inc., Miami, Fla., June 12-17. Dr. Lorand V. Johnson, 10515 Carnegie Ave., Cleveland 6, Secretary-Treasurer.

Endocrine Society, Eden Roc Hotel, Miami Beach, Fla., June 9-11. Dr. Henry H. Turner, 1200 N. Walker, Oklahoma City, Okla., Executive Secretary.

Idaho State Medical Association, Sun Valley, June 15-18. Mr. Armand L. Bird, Sonna Bldg., Boise, Idaho, Executive Secretary.

Maine Medical Association, Hotel Samoset, Rockland, June 19-21. Dr. Daniel F. Hanley, P. O. Box 240, Brunswick, Maine, Executive Director.

Northwest Proctologic Society, Roche Harbor, San Juan Island, Wash., June 21-24. Dr. L. D. Leslie, 1162 Willamette St., Eugene, Ore., Secretary-Treasurer.

Society of Biological Psychiatry, Deauville Hotel, Miami Beach, Fla., June 11-12. Dr. George N. Thompson, 2010 Wilshire Blvd., Los Angeles 57, Executive Secretary.

Society for Investigative Dermatology, Inc., di Lido Hotel, Miami Beach, Fla., June 13-15. Dr. Herman Beerman, 255 S. 17th St., Philadelphia 3, Secretary-Treasurer.

Society of Nuclear Medicine, Estes Park, Colo., June 22-25. Dr. Thad P. Sears, Veterans Administration Hospital, Denver 20, Chairman.

Society for Vascular Surgery, di Lido Hotel, Miami Beach, Fla., June 12. Dr. George H. Yeager, 314 Medical Arts Bldg., Baltimore 1, Secretary.

July

American Goiter Association, Church House, London, England, July 5-8. Dr. John C. McClintock, 702 Madison Ave., Albany 8, N. Y., Secretary.

American Society of Facial Plastic Surgery, Hotel Elysee, New York City, July 22. Dr. Samuel M. Bloom, 123 E. 83d St., New York 28, Secretary.

Flying Physicians Association Hawaii Cruise, leaving Los Angeles and San Francisco, July 11. For information write Mr. Mark E. DeGroff, P. O. Box 3275, Tulsa, Okla.

Oregon Cancer Conference (Second Annual), Sheraton Hotel, Portland, July 7-8. Dr. Martin A. Howard, 115 S. W. Taylor St., Portland 5, Ore., Chairman.

Rocky Mountain Cancer Conference, Hilton Hotel, Denver, July 20-21. Mr. Harvey T. Sethman, 835 Republic Bldg., Denver 2, Executive Secretary, Colorado State Medical Society.

American Association of Blood Banks, Jack Tar Hotel, San Francisco, Aug. 21-26. For information write: AABB Central Office, Suite 1619, 30 N. Michigan, Chicago 2.

American Congress of Physical Medicine and Rehabilitation, Mayflower Hotel, Washington, D. C., Aug. 21-26. Mrs. Dorothea C. Augustin, 30 N. Michigan Ave, Chicago 2, Executive Secretary.

American Hospital Association, Civic Auditorium, San Francisco, Aug. 27-Sept. 1. Mr. Maurice J. Norby, 18 E. Division St., Chicago, Assistant Director.

American Institute of Ultrasonics in Medicine, Statler-Hilton Hotel, Washington, D. C., Aug. 20. Dr. Dorothy M. Stillwell, Dept. of Phys. Med. and Rehab., Univ. of Colorado Med. Center, Denver 20, Chairman.

American Physiological Society, Stanford University, Calif., Aug. 22-26. Mr. Ray G. Daggs, 9650 Wisconsin Ave., Washington 14, D. C., Executive Secretary.

American Society of Clinical Hypnosis, Miami, Fla., Aug. 7-10. Dr. Seymour Hershman, 6770 N. Lincoln Ave., Chicago 46, Secretary.

American Veterinary Medical Association, Denver-Hilton Hotel, Denver, Aug. 15-18. H. E. Kingman Jr., 600 S. Michigan Avenue, Chicago 5, Executive Secretary.

Biological Photographic Association, Inc., Utah Motor Lodge, Salt Lake City, Utah, Aug. 23-26. Miss Jane H. Waters, Box 1668, Grand Central P. O., New York 17, Executive Secretary.

Conference on the Chemical Organization of Cells: Normal and Abnormal, University of Wisconsin, Madison, Aug. 25-27. Dr. J. F. A. McManus, Dept. of Pathology, University of Alabama Medical Center, Birmingham, Chairman.

Gerontological Society, Inc., Mark Hopkins Hotel, San Francisco, Aug. 7-12. Mrs. Marjorie Adler, 660 S. Kingshighway Blvd., St. Louis 10, Administrative Secretary.

National Medical Association, Inc., Penn-Sheraton Hotel, Pittsburgh Aug. 8-11. Dr. John T. Givens, 1108 Church St., Norfolk, Va., Executive Secretary.

Reno Surgical Society, Mapes Hotel, Reno, Nev, Aug. 18-20. Dr. Gilbert G. Lenz, 505 S. Arlington Ave., Reno, Nevada.

Rocky Mountain Radiological Society, Denver-Hilton Hotel, Denve Aug. 11-13. Dr. John H. Freed, 4200 E. 9th Ave., Denver 20, Secretar Treasurer.

St. Joseph's Hospital Annual Clinics, St. Joseph's Hospital, Denve Aug. 3-5. Dr. W. H. Leitch, St. Joseph's Hospital, 1818 Humboldt S Denver 18, Chairman.

West Virginia State Medical Association, The Greenbrier, Whi Sulphur Springs, Aug. 25-27. Mr. Charles Lively, Box 1031, Charlest 24, W. Va., Executive Secretary.

September

American Academy of Pediatrics, and American Academy of Ge eral Practice, Louisiana Chapter, Roosevelt Hotel, New Orlea Sept. 23. Dr. Herbert B. Rothschild, 1520 Louisiana Ave., New Orle 15, Chairman of Publicity Committee.

American Medical Writers' Association, Hotel Morrison, Chica Sept. 30-Oct. 1. Dr. Harold Swanberg, 510 Maine St., Quincy, Secretary.

American Roentgen Ray Society, Ambassador Hotel, Atlantic C Sept. 27-30. Mr. Hugh Jones, 20 N. Wacker Dr., Chicago 6, Direc Public Relations.

American Society of Clinical Pathologists, Palmer House, Chic Sept. 24-Oct. 2. Mr. Claude E. Wells, 445 Lake Shore Drive, Chic 11, Executive Secretary.

College of American Pathologists, Palmer House, Chicago, Sept. 27. Dr. Arthur H. Dearing, 2115 Prudential Plaza, Chicago, Execu Director.

Colorado State Medical Society, Stanley Hotel, Estes Park, Sept. 17. Mr. Harvey T. Sethman, 835 Republic Bldg., Denver 2, Execu Secretary.

Delaware, Medical Society of, Rehoboth, Del., Sept. Mr. Law C. Morris Jr., 1925 Lovering Ave., Wilmington 6, Del., Execu Secretary.

Flying Physicians Association, third clinical meeting, Western Lodge, Wagoner, Okla., Sept. 6-9. For information write: Flying P cians Association National Headquarters, P. O. Box 3275, Tulsa,

Inter-Society Cytology Council, Palmer House, Chicago, Sept. 2 Dr. Paul A. Younge, 1101 Beacon St., Brookline 46, Mass., Secre

Kentucky State Medical Association, Louisville, Sept. 20-22. J. P. Sanford, 1169 Eastern Parkway, Louisville 17, Ky., Exec Secretary.

Maryland, Medical and Chirurgical Faculty of the State Semiannual Meeting, Ocean City, Sept. 16. Mr. John Sargeant, Cathedral St., Baltimore 1, Executive Secretary.

Michigan State Medical Society, Detroit, week of Sept. 25. D Bruce Wiley, 606 Townsend St., Lansing 15, Mich., Secretary.

Montana Medical Association, Baxter Hotel, Bozeman, Sept. Dr. William E. Harris, 114 N. Second, Livingston, Montana, Secr

National Cancer Conference, American Cancer Society, Inc., the National Cancer Institute, Minneapolis, Minnesota, Sept 15. Dr. Roald M. Grant, 521 W. 57th St., New York 19, Coordi

National Recreation Congress, Shoreham Hotel, Washington, Sept. 25-29. Willard B. Stone, 8 W. Eighth St., New York 11, Secr

Nevada State Medical Association, Stardust Hotel, Las Vegas, 7-10. Mr. Nelson B. Neff, P. O. Box 2790, Reno, Nev., Exe Secretary.

New England Society of Anesthesiologists, Bretton Woods, Sept. 18-19. Dr. Thomas K. Burnap, P. O. Box 81, Kenmore S P. O., Boston 15.

Oregon State Medical Society, Portland, Sept. 7-9. Mr. Rosc Miller, 2164 S. W. Park Place, Portland 5, Ore., Executive Secret

Pacific Dermatologic Association, Empress Hotel, Victoria, Columbia, Canada, Sept. 1-4. Dr. Edward J. Ringrose, 2636 Tel Ave., Berkeley 4, Calif., Secretary-Treasurer.

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DRUG USAGE AND ANTIBIOTIC SUSCEPTIBILITY OF STAPHYLOCOCCI

Alfred W. Bauer, M.D., David M. Perry, M.D.
and
William M. M. Kirby, M.D., Seattle

A technique whereby a given strain of bacteria can be tested for sensitivity against 12 to 15 antibiotics simultaneously on a single plate was used in a study of resistance to drugs among staphylococci cultured from hospital inpatients and outpatients. Within the period 1955 through 1959, resistance to penicillin changed but little from the level of 60 to 80% previously attained. Resistance to streptomycin remained stable at about 55%. Resistance to tetracyclines, chloramphenicol, and erythromycin was considerable, but mutants resistant to neomycin, bacitracin, vancomycin, ristocetin, and kanamycin were not observed. The data supported the concept that the greater the amount of a drug consumed the greater the likelihood of encountering resistant strains. They also confirmed reports that chloramphenicol had much less effect in inducing the emergence of resistant strain than did the other antibiotics tested.

NUMEROUS publications dealing with the phenomenon of emergence of drug-fastness among staphylococci have appeared in the literature of many countries, and xcellent reviews concerning the different aspects f the problem are available.[1] In an earlier publicaion,[2] data from the King County Hospital for the ears 1951 to 1953 were reported. Particularly ineresting was the decline in chloramphenicol resistnce from 20 to 6% after a temporary restriction 1952-1953) in the use of this agent in the hospital. The purpose of the present study is to offer followup information concerning the incidence of antibiotic resistance from 1955 through 1959. Special consideration will be given to the correlation between drug consumption in the hospital and the magnitude of resistance among staphylococci cultured from inpatients. "Outside" staphylococci will be compared with hospital strains, and the unique situation which exists with chloramphenicol regarding drug use and emergence of resistance will be discussed in detail.

A technique of sensitivity-testing in which a single antibiotic disk is used, with measurement of zone diameters, has been in use at the King County Hospital for several years.[3] Additional information and experience have been obtained, leading to some modifications in interpreting the tests, and a new presentation and discussion of this simple and accurate procedure therefore seems appropriate.

From the Department of Medicine, University of Washington School of Medicine, and the King County Hospital.

Material and Methods

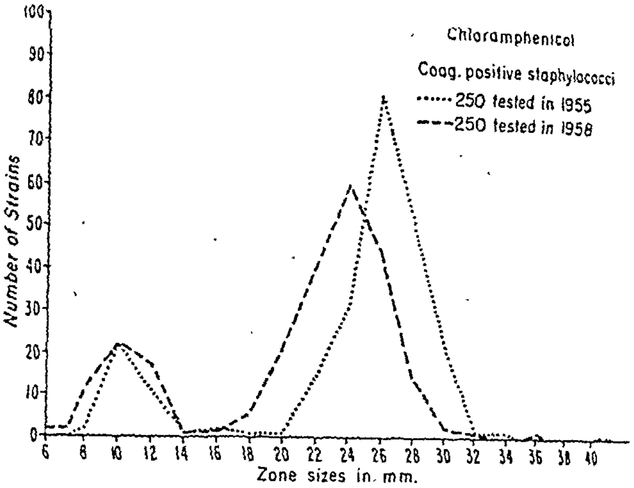
Micro-organisms.—All staphylococci in the present study were cultured during the years 1955 through 1959 in the routine diagnostic laboratory of the King County Hospital from patients or carriers on the wards, and from patients in the emergency room. The results of sensitivity tests of 250 strains consecutively isolated from inpatients and of 50 to 100 cultured in the emergency room during the summer months of each year 1955 through 1959 were selected as a representative sample. Only coagulase-positive staphylococci were included.

Sensitivity-Testing Method.—Details of the method have been described elsewhere.[4] Briefly, large Petri dishes (15 cm.) which will accommodate 10 to 12 antibiotic disks were used, and Mueller-Hinton agar was the medium used for all tests. Bacterial growth from a broth subculture was spread evenly over the surface of the medium with a cotton swab, and disks were placed on the agar as soon as the inoculum had dried. One disk was used for each antibiotic, and after incubation overnight at 37 C the entire diameter of the zone of inhibition of growth was measured, including the 6 mm. disk. In table 1 the antibiotic content of the disks and the standards for interpretation of zone sizes are presented. Since each antibiotic has a different diffusion capacity, the zone sizes indicating varying degrees of susceptibility are different for each agent.

Validity of Method.—As is true of others[5] who have had extensive experience with a single high-content disk for each antibiotic, with measurement of zone diameters, we have found a good correlation between antibiotic susceptibility of bacteria and the diameter of inhibition zones about antibiotic disks. In our experience most staphylococci fall into two well separated groups, sensitive or resistant, and strains of intermediate susceptibility are uncommon. This biological phenomenon of two clearly separated groups has been documented in detail in our earlier publication,[4] and is illustrated in the figure. The distribution curves for chloramphenicol susceptibility of 250 staphylococci from 1955 and 250 from 1958 are shown. The ordinate in the figure gives the number of strains and the abscissa the zone diameters in millimeters. Two peaks for each year are clearly shown (bell-shaped curves, if more measuring points are used) representing the sensitive population on the right and the resistant group on the left. The zone sizes of susceptible strains recorded in 1955 were larger than in 1958 because of the use of 60-mcg., as opposed to 30-mcg., disks. Resistant organisms (i. e., resistant to antibiotic concentrations ordinarily obtained in the serum of patients) have small zones or no zone of growth inhibition, while sensitive strains have large zones. On the average, only one strain in a hundred falls into the intermediate range, with a zone diameter of between 13 and 17 mm. In our earlier report,[4] the division lines obtained from distribution curves were shown to correlate well with the results of comparative tube dilution tests. For the purpose of separating the resistant from the sensitive organisms, our studies have shown that the single disk technique is as accurate as the tube dilution test and is much simpler to perform.

TABLE 1.—*Zone Diameters in Millimeters as Standards for Interpretation of Single Disk Tests*

Antibiotic		Bacterial Susceptibility		
Type	Amount	Resistant	Intermediate	Sensitive
Tetracycline	30 mcg.	6-14	15-18	>18
Chloramphenicol	30 mcg.	6-12	13-17	>17
Streptomycin	100 mcg.	6-20	21-22	>22
Polymyxin B	30 mcg.	6-9	...	>9
Penicillin	10 units	6-20	21-28	>28
Erythromycin	15 mcg.	6-14	15-18	>18
Bacitracin	20 units	6-8	9-12	>12
Sulfisoxazole	300 mcg.	6-8	9-14	>14
Neomycin	30 mcg.	6-8	9-11	>11
Oleandomycin	15 mcg.	6-11	12-16	>16
Nitrofurantoin	300 mcg.	6-8	9-12	>12



Distribution curves showing clear-cut differentiation between resistant and susceptible staphylococci as determined by single disk method.

Reproducibility of Test Results.—In addition to a good correlation with tube dilution test procedures, the single disk test shows excellent reproducibility of results. In table 2 inhibition zone sizes are shown for a strain of Staphylococcus aureus, bacteriophage type 80/81, which was isolated 9 times from a patient with septicemia and tested on 13 separate occasions under routine conditions for antibiotic sensitivity. The cultures were obtained on different days and from different sites and were tested without reference to previously recorded sensitivities. The organism was resistant to penicillin, streptomycin, and tetracycline and sensitive to all the other agents listed. Despite some variations in zone sizes due to differences in inoculum size and other technical variants, the interpretation (see table 1) was the same on each occasion with the exception of the culture from Oct. 16, 1958, when the organism was recorded as "intermediate" (zone size 22 mm.) instead of resistant to streptomycin. Thus, of the 117 separate measurements recorded in table 2, 116 yielded a correct result. It might be desirable on some occasions to retest the "intermediates." In our experience most of them are the result of a light inoculum and fall into the resistant group when retested.

Results

Staphylococci from Inpatients.—Table 3 shows the percentage of antibiotic-resistant coagulase-positive organisms isolated from inpatients and from emergency room patients from 1955 through 1959. Emergency room strains are labeled as "outside" strains, although patients in the emergency room of a county hospital probably have had more contact with the hospital environment than the average of the community at large. To provide a proper background for comparison, sensitivity reports from several other sources are summarized in table 4, covering the years 1950 through 1957. Data regarding each antibiotic will be considered separately.

Table 2.—*Results of Sensitivity Tests of Staphylococcus Cultured on Nine Occasions from One Patient During Fourteen-Day Hospital Course*

Date, Oct., 1958	Source of Culture	Antibiogram (Mm. Zone Diameter)* T	O	C	S	P	E	B	N	F	Bacteriophage Type
16th	Blood Broth	9	23	21	12	8	26	19	24	14	80/81
	Pour plate	11	25	24	15	11	28	23	25	18	
16th	Blood Broth	9	22	21	12	6	23	18	19	15	80/81
	Pour plate	9	24	23	14	12	27	21	25	16	
16th	Skin	10	20	19	22	6	19	19	21	16	80/81
16th	Urine	11	19	20	10	6	20	18	20	14	80/81
17th	Blood Broth	6	29	28	17	12	31	23	28	19	80/81
	Pour plate	9	23	25	14	6	28	20	23	19	
21st	Blood Broth	10	26	29	16	6	29	21	23	20	80/81
23rd	Blood Broth	11	25	26	12	14	28	23	25	17	80/81
	Pour plate	6	27	28	15	7	29	21	24	19	
25th	Blood Broth	11	26	22	15	12	30	21	25	18	
27th	Blood Broth	12	25	25	15	6	31	25	28	20	80/81

*T = tetracycline, O = oleandomycin, C = chloramphenicol, S = streptomycin, P = penicillin, E = erythromycin, B = bacitracin, N = neomycin, F = nitrofurantoin.

Penicillin.—Resistance to penicillin among staphylococci isolated from hospitalized patients (or from various sources combined in some instances as shown in table 4) had reached a level of 60 to 80% by 1950, and has remained essentially unchanged from that time to the time of this writing. Since 1955 we have recorded a yearly resistance rate of about 80% in the hospital. Data from Europe, Africa, Asia, and America (table 4) are similar. It would appear that an equilibrium has been established in the rates of emergence and disappearance of resistant organisms.

Streptomycin.—Reports in the literature indicate that resistance to this antibiotic was, in general, below 50% up to 1953 and has been between 50 and 70% since 1954. Our own incidence of resistance has been stable at about 55% since 1955.

Tetracyclines.—Up to 10% of staphylococci were resistant to the tetracyclines in 1950. The percentage increased to a level of 40 to 60% by 1953, and has been relatively constant since then. In our own material 42% of strains were resistant in 1952. The percentage increased to 67 in 1955 and 1956 and has dropped since then for reasons that will be considered later.

Chloramphenicol.—About a 20% incidence of resistant strains was recorded by some authors as early as 1951. In 1952 and 1953 there was a decline to figures below 10% coincident with a general decrease in use of this antibiotic. As drug consumption increased again, the resistance rate has also risen. Most authors, however, have reported less than 20% of resistant organisms. At the King County Hospital, where an unusually large amount of chloramphenicol has been used, the percentage of resistant organisms seems to have leveled off between 20 and 30%.

Erythromycin.—Emergence of resistance was first noted in 1953, and in later years 10 to 30% of resistant strains have been reported. Our own data indicate that erythromycin resistance has increased up to 30% since 1958.

Table 3.—*Sensitivity Pattern of Staphylococci, King County Hospital, 1955-1959*

		Strains*						
		Inpatient, %†			Outside, %			
Antibiotic	Yr.	R	I	S	No.	R	I	S
Penicillin	1955	81	1	18	50	74	6	20
	1956	83	2	15	50	72	6	22
	1957	77	5	18	50	70	6	24
	1958	77	2	21	100	61	7	32
	1959	78	1	21	60	63	3	34
Streptomycin	1955	60	13	27	50	38	16	46
	1956	59	16	25	50	32	24	44
	1957	52	9	39	50	34	14	52
	1958	56	13	31	100	31	19	50
	1959	52	3	45	60	28	7	65
Tetracycline	1955	67	0	33	50	42	0	58
	1956	67	0	33	50	30	0	70
	1957	42	0.5	57.5	50	57	0	44
	1958	53	0.5	46.5	100	34	0	66
	1959	44	1	55	60	29	0	71
Chloramphenicol	1955	14	1	85	50	4	0	96
	1956	33	0.5	66.5	50	0	0	100
	1957	22	2	76	50	4	0	96
	1958	22	1	77	100	4	1	95
	1959	21	1	78	60	5	0	95
Erythromycin	1955	14	1	85	50	6	0	94
	1956	24	0.5	75.5	50	4	0	96
	1957	25	6	69	50	20	2	78
	1958	31	6	63	100	14	5	81
	1959	31	1	68	60	13	0	87

* R = resistant, I = intermediate, S = sensitive. All strains were coagulase-positive.

† Two hundred fifty strains were tested in each group.

Resistance to Other Antibiotics.—Mutants resistant to neomycin, bacitracin, vancomycin, ristocetin, and kanamycin have not been observed so far in this hospital, the use of these agents being rather limited. Resistance to novobiocin is below 3%. Again, this antibiotic has been used very little and only about 200 strains have been tested so far. Oleandomycin has been used infrequently and resistance to this drug (about 3%) presumably has been noted because of cross-resistance with erythomycin. In our experience, cross-resistance between erythromycin and oleandomycin has been considerably more frequent among coagulase-negative strains. Coagulase-positive staphylococci have been consistently sensitive to nitrofurantoin in our laboratory; no resistant strains have been detected among several thousand isolates tested since 1955.

Incidence of Resistance in Staphylococci from Patients Admitted to Emergency Room.—The incidence of antibiotic resistance was generally lower among isolates from emergency room patients than from inpatient sources. Most impressive was the fact that only 12 chloramphenicol-resistant strains were found among 310 of these strains from patients treated in the emergency room. When these 12 cultures were traced to their origin it was found that all of them were derived from patients with recent extensive contact with the hospital. One patient had made 40 visits to the outpatient clinics and the emergency room during preceding months. Others had been discharged from the wards a few days or weeks prior to the emergency room visit when their old lesions were cultured. Five of the 12 patients were hospital employees with purulent skin infections. All three patients in this group in 1959 were hospital employees with purulent skin infections treated in the emergency room.

TABLE 4.—*Antibiotic Resistance of Staphylococci as Reported from Several Authors, 1950-1957 (Numbers Indicate Percentage of Resistant Strains)*

	Antibiotic*									
Author & Year	Penicillin	Streptomycin	OT	CT	T	OT & CT	CT & T	Chloramphenicol	Erythromycin	Technique
1950										
Kenney	70	9	1	9	..	..	..	0	..	Single disk
Leyton	53	..	..	23	..	..	..	..	..	Tube dilution
Spink	55	19	2	6	..	..	..	7	..	Tube dilution
1951										
Wise	62	48	38	23	..	..	..	25	..	Tube dilution
Kenney	88	18	14	17	..	..	..	8	..	Single disk
Leyton	61	10	..	28	..	..	..	<10	..	Tube dilution
Kirby (51/52)	73	..	..	..	..	42	..	20	..	Single disk
Finland (51/52)	73	10	32	24	..	..	..	2	..	Plate dilution
Meleney (51/52)	37	2.5	10	..	..	..	..	..	..	Single disk
1952										
Goetz (Germ.)	60	40	..	..	..	..	..	..	..	Plate dilution
Wise	57	19	47	33	..	..	..	2.5	0	Tube dilution
Kenney	80	25	30	30	..	..	..	11	..	Single disk
Meleney (52/53)	44	30	38	..	..	..	..	..	..	Single disk
1953										
Goetz (Germ.)	50	25	..	..	..	5	..	<1	<1	Plate dilution
Wise	63	65	..	..	..	63	..	0.65	21	Tube dilution
Kirby	68	..	..	..	..	61	..	6	2	Single disk
Gupta (India)	10	5	..	73	36	..	..	6	..	Single disk
Royer (Canada)	72	48	30	15	..	..	..	11	32	Several techniques
Rantz (50-53)	70	45	..	..	42	..	..	8	..	Plate dilution
1954										
Goetz (Germ.)	88	45	21	24	..	..	..	5	4	Plate dilution
Sompolinsky (Israel)	90	75	..	..	..	8	..	0	..	Single disk
Royer (Canada)	64	58	54	25	..	..	..	10	23	Several techniques
Spink	73	70	60	66	56	..	..	0.78	15	Tube dilution
Rantz	80	46	..	..	48	..	..	10	3	Plate dilution
1955										
Goetz (Germ.)	80	58	..	..	40	..	..	20	13	Plate dilution
Royer (Canada)	82	58	..	34	50	..	..	11	25	Several techniques
Spink	71	69	56	52	50	..	..	2	22	Tube dilution
Rantz	82	52	..	..	52	..	..	3	11	Plate dilution
1956										
Goetz (Germ.)	82	61	..	..	46	..	..	10	2	Plate dilution
Koch	..	..	..	..	..	..	..	19	..	Single disk
Hennessey (Afr.)	65	22	..	..	..	..	4	2	0.5	"Sentest" tablets
Walsbren (52-56)	75	65	56	..	..	..	52	12	23	Tube dilution
Royer (Canada)	60	42	..	..	45	40	..	8	17	Several techniques
1957										
Petersdorf	72	..	..	..	70	..	..	14	26	Tube dilution
Cheng (China)	71	60	..	..	..	46	..	..	..	Tube dilution
Royer (Canada)	56	46	48	..	42	..	..	8	16	Several techniques

* OT = oxytetracycline; CT = chlortetracycline; T = tetracycline.

The percentage of resistance to other antibiotics also was lower among outpatients but the differences were not as striking as with chloramphenicol. Resistance to tetracycline from 1955 through 1959 was between 30 and 50%, only slightly lower than in the hospital. Erythromycin resistance was definitely lower in outpatients but showed a moderate increase during the four-year period. Streptomycin resistance of strains from patients treated in the emergency room remained unchanged at about 35%, definitely lower than that of inpatients. Resistance to penicillin had the highest incidence, the figure of 60 to 70% being only slightly lower than the 80% consistently recorded from inpatient sources.

Influence of Drug Consumption.—As summarized in table 5, there was a surprisingly good correlation between drug consumption in the hospital and the rate of resistance among staphylococci isolated from inpatients. Only figures for tetracycline, chloramphenicol, and erythromycin were available. The decrease in tetracycline resistance from 1956 to 1957 was preceded by a 50% decrease in drug consumption. A twofold increase in chloramphenicol usage from 1955 to 1956 was associated with a corresponding increase in resistance to this agent.

Despite a further increase in use, the percentage of chloramphenicol-resistant strains has actually been lower in subsequent years. A steady rise in erythromycin consumption from 1954 to 1957 has been associated with a continuous increase in resistance to this antibiotic until 1958. During the past year, the use of this antibiotic has decreased slightly and there has been no further rise in resistance.

Comment

Although it has been generally recognized that use of antibiotics and emergence of resistance are correlated, few data can be found in the literature which document the exact relationships for various antibiotics. Some authors have even challenged the existence of a direct correlation between antibiotic consumption and bacterial resistance. For example, Waisbren[6] demonstrated differences in resistance rates among staphylococci cultured from different sites of the body (e. g., blood cultures versus wound cultures), from different hospitals in the community, and from interns as compared with patients. He also noted that chloramphenicol susceptibility varied seasonally, strains isolated during summer months being less sensitive than "cold-weather strains." In each instance the bacteria were thought to have been under identical "antibiotic pressure." The author concluded that drug consumption is probably only one of the factors involved in antibiotic resistance of staphylococci, if a factor at all. Our own data do not support this conclusion. For example, we have found no difference in chloramphenicol resistance of staphylococci isolated in winter and in summer months. Of 250 strains cultured in July and August, 1957, 22% were resistant, as compared with 24% resistant strains among 250 isolates tested in January and February, 1958.

Our paper not only supports the concept that there is a close relationship between drug consumption and resistance to antibiotics but also provides evidence of the degree to which different drugs influence bacterial susceptibility in a hospital environment. Particularly striking was the fact that the use of chloramphenicol in the hospital had much less effect, on a weight basis, on the emergence of resistance than did the consumption of tetracycline and erythromycin. Roughly speaking, each additional kilogram of chloramphenicol used per year in the hospital was associated with a 1% increase of chloramphenicol resistant strains, whereas an increase or decrease of 1 kg. of tetracycline or erythromycin per year was paralleled by a rise or decline of 4 to 5% in the resistance rate to these agents. Since the average daily doses of all three drugs are similar, chloramphenicol-resistant mutants seemed to emerge less frequently or to disappear more readily, or both, than strains resistant to tetracycline or erythromycin. There are a number of reports available in the literature which confirm the relatively low incidence of chloramphenicol-resistant staphylococci in hospitals. Indeed, the rate seems to have reached a plateau at about 20 to 30% and indications are that it may not go higher despite increased use. Furthermore, it has been shown that the resistance rate in hospitals declines rapidly when use of chloramphenicol is decreased. Gibson and Thompson,[7] for example, set up a rotational program of drug use on two wards with patients suffering from burns and recorded its effect on susceptibility of staphylococci. They found that resistance to chlortetracycline persisted at high levels long after this agent was discontinued, while chloramphenicol resistance dropped rapidly to 1 to 4% after it was stopped. Our own data[2] showed a decline in chloramphenicol resistance from 20 to 6% when the use of this antibiotic was curtailed in 1953.

TABLE 5.—*Correlation Between Drug Consumption in Hospital and Rate of Resistance Among Staphylococci Isolated from Inpatients of King County Hospital*

	Consumption of Antibiotic		Resistant Strains	
	Date	Kg.	Date	%
Tetracycline	July, 1954—June, 1955	21.9	July-Aug. 1955	67
	July, 1955—June, 1956	13.6	July-Aug. 1956	67
	July, 1956—June, 1957	10.1	July-Aug. 1957	42
	July, 1957—June, 1958	11.1	July-Aug. 1958	53
	July, 1958—June, 1959	9.3	July-Sept. 1959	44
Chloramphenicol	July, 1954—June, 1955	10.4	July-Aug. 1955	14
	July, 1955—June, 1956	23.2	July-Aug. 1956	33
	July, 1956—June, 1957	25.1	July-Aug. 1957	22
	July, 1957—June, 1958	27.4	July-Aug. 1958	22
	July, 1958—June, 1959	22.2	July-Sept. 1959	21
Erythromycin	July, 1954—June, 1955	2.7	July-Aug. 1955	14
	July, 1955—June, 1956	5.1	July-Aug. 1956	24
	July, 1956—June, 1957	7.5	July-Aug. 1957	28
	July, 1957—June, 1958	6.7	July-Aug. 1958	31
	July, 1958—June, 1959	5.1	July-Sept. 1959	31

The present study shows that the same relatively unique situation exists with regard to strains from outpatients as well as inpatients. Resistance to chloramphenicol was rare among staphylococci isolated from outside sources (0-5%) as compared with inpatients (20-30%). With penicillin, tetracycline, erythromycin, and streptomycin there was also a lower rate of resistance among "outside strains," but the differences were much less striking. The most likely explanation seems to be that chloramphenicol-resistant staphylococci disappear more readily after leaving the hospital environment. Similar observations were made in a study recently published by Goslings and Büchli.[8] These authors observed the incidence of nasal carriers of staphylococci in surgical patients in Leyden, Holland, before and after discharge from the hospital with determination of antibiogram and bacteriophage type. They found that chloramphenicol resistance disappeared more rapidly than did resistance to other antibiotics. This was attributed by the authors to back-mutation of resistant strains to susceptibility and to replacement of resistant bacteria by sensitive strains of other bacteriophage types. Thus, it is likely that chloramphenicol-resistant strains are genetically unstable and have a decreased ability to survive when competing with other strains in the absence of the drug. Strains resistant to tetracycline and streptomycin disappeared more slowly in the Leyden study, while penicillin-resistant organisms remained for the longest period in the noses of discharged patients. This may account in part for the high incidence of penicillin resistance among outpatients. Of course, the widespread use of penicillin and the tetracyclines in home and office practice may also be a contributing factor in maintaining a high resistance rate among staphylococci.

Summary

A single disk technique for bacterial antibiotic sensitivity testing has provided the data on which the present report is based. This technique has been in use at the King County Hospital for several years, and has consistently shown good correlations with tube dilution tests, and with the clinical response to therapy. Slight modifications in technical procedures and interpretations have been introduced and these are described briefly in the present report.

Data concerning susceptibility of staphylococci cultured at the King County Hospital from 1955 through 1959 to a series of commonly used antibiotics were compared with sensitivity reports from other sources.

Penicillin resistance was found in about 80% of staphylococci cultured from inpatients; this has not changed materially since 1950. Resistance to streptomycin has remained between 50 and 70% since 1954 and to tetracycline between 40 and 60% since 1953. Erythromycin resistance has gradually increased to over 25%. Chloramphenicol resistance has been reported at below 20% by most authors; it was found to be between 20 and 25% in this hospital, in which large amounts of the drug are used.

Definitely lower percentages of resistance were seen among strains of staphylococci isolated from patients treated in the emergency room, with penicillin (60-70%), streptomycin (30-40%), and tetracycline (20-50%) showing the highest rates. Resistance to chloramphenicol was surprisingly infrequent (0-5%).

Correlations between antibiotic consumption in the hospital and the incidence of drug resistance were documented. Chloramphenicol was less effective on a weight basis in inducing resistance among "hospital staphylococci" than was tetracycline or erythromycin. An increase in consumption of 1 kg. of chloramphenicol from year to year in a 380-bed hospital was paralleled by an increase of 1% of resistant strains, while each additional kilogram of tetracycline or erythromycin used was associated with an increase of 4 to 5% of isolates resistant to these agents.

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NORMAL BEHAVIOR.—No valid comparative statistics of the incidence of mental illness in different parts of the world is possible today because of the great differences in social attitudes as to what constitutes mental illness or abnormal behavior in different countries. What is considered as manifestation of severe mental illness in one culture may be looked upon, in a culture with a more primitive outlook, as a high form of religious attainment. Thus, comparative surveys of the attitudes of the peoples toward variations in human behavior and toward facilities and techniques for the treatment of those considered mentally ill are basic to a genuine international epidemiological study of mental illness and mental health. —F. Fremont-Smith, M.D., World Mental Health Year, *Hospital Progress*, February, 1960.

RADIOACTIVE IRON TECHNIQUES IN CLINICAL PRACTICE

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The rate at which intravenously injected iron disappears from the blood depends partly on the rate at which iron is being used for the production of fresh erythrocytes in the bone marrow. The injection of radioactive iron (Fe^{59}) has proved to be a convenient means of measuring the rate of disappearance of iron from the plasma and its uptake by the erythrocytes. Experience has led to the use of 4 microcuries of Fe^{59} in the form of ferrous citrate as the standard injection. The data accumulated have been shown to be useful in the diagnosis of aplastic anemia, iron deficiency anemia, leukemia, and polycythemia. Since continuing losses of blood and variations in the iron stores of the body affect the results, intelligent interpretation is required.

It is the purpose of this communication to describe radioiron techniques performed in the radioisotope department of Bellevue Hospital and to indicate their usefulness in clinical practice.

The techniques described are modifications of those introduced by Huff and co-workers [1] in 1950 and subsequently elaborated by others.[2] Our modifications have been made with two goals in mind: that the test be simple and easily reproducible in any clinical or radioisotope laboratory without dependence on highly developed laboratory skills or specialized equipment; and that the patient be subjected to minimal inconvenience.

Two tests are performed routinely in this laboratory: the plasma clearance rate of injected radioactive iron (Fe^{59}) and the eight-day erythrocyte uptake of Fe^{59}.

The performance of these tests is somewhat similar to the techniques used by Loeffler and his group [3] in the United States and Wetherley-Mein and co-workers [4] in England. Though neither of these groups claim originality for the techniques, it is to their credit that they have been among the first to remove the tests from the realm of research tools to that of routine hematological practice.

Technique

The steps necessary to determine the plasma clearance rate and eight-day uptake of injected Fe^{59} citrate are as follows: 1. Dilute about 5 μc of Fe^{59} citrate with 5 cc. of isotonic sodium chloride solution. 2. Rapidly inject the above preparation (diluted Fe^{59}) intravenously. 3. Withdraw 5 cc. of whole-blood samples at 5, 15, 30, 60, 90, and 120 minutes into oxalated tubes; pipet 4 cc. of each sample of whole blood into counting tubes. 4. Count all specimens in a well scintillation counter and correct for background radioactivity. 5. Plot whole-blood activity in net counts against time on semilog paper, with radioactivity counts on the logarithm scale, and time on the linear scale. 6. Extrapolate the straight line obtained to zero time; locate the 50% point which indicates the plasma clearance half-time. 7. Eight days later, withdraw 15 cc. of a whole-blood specimen into an oxalated tube. 8. Count 4 cc. of the whole blood in a well scintillation counter and spin down the remainder to obtain plasma and hematocrit values. 9. If

k = 8-day correction factor for radioactive decay = 1.12,
then
U = 8-day uptake of Fe^{59} by erythrocytes = $k \times C_{W8} \times C_{W0}$
where
C_{W8} = counts per 4 cc. of whole blood on the eighth day
and
C_{W0} = 100 times the number of counts per 4 cc. of whole blood, extrapolated to zero time as directed in step 6.

10. Count 4 cc. of the eight-day plasma specimen obtained in step 8. If the counts obtained are more than 15% of the eight-day whole blood specimen, correct the value of U obtained in step 9 above by multiplying by a factor F obtained as follows:

$$F = (C_{W8} - C_{P8} + h) \times C_{P8}$$

where
C_{P8} = count per 4 cc. of plasma on the eighth day
and
h = hematocrit = cubic centimeters of packed erythrocytes obtained from 1 cc. of whole blood.

Comment

Radioactive iron injected into the blood stream as ferrous citrate is cleared at an exponential rate. If samples of blood taken at intervals up to two hours are counted in a well scintillation counter, the results plotted on semilogarithmic paper form a straight line, representing the rate at which radioactivity is cleared out of the blood. In the normal person, between 65 and 110 minutes are

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From the Radioisotope Department, Bellevue Hospital, and the Department of Radiology, New York University College of Medicine.

required for the radioactivity to fall to one-half of what it was at zero time. This is referred to as "the plasma clearance one-half time" (fig. 1).

This plasma clearance test is easy to perform. It requires (1) a series of venipunctures, (2) tubes containing anticoagulants, and (3) a well scintillation-counter system.

The eight-day red blood cell uptake (RBCU) of Fe^{59} is equally easy to determine, requiring only the count of a single sample of oxalated blood, withdrawn at eight days. Measurement of whole-blood samples in the same manner of calculation, without standards, dilutions, hematocrits, and cell volumes makes the procedure simple and reproducible.

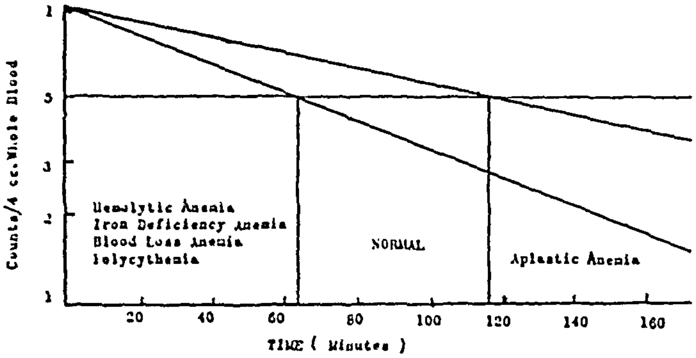

Fig. 1.—Plasma clearance curve of radioactive iron (Fe^{59}) citrate. If, after intravenous injection of Fe^{59} citrate, radioactivity in one aliquot of whole blood is measured at intervals and plotted on semilog paper, a straight line indicating exponentially that the Fe^{59} is being cleared out of the blood is obtained. Rapid clearance occurs in polycythemia, hemolytic anemia, iron deficiency anemia, and blood loss anemia; slow clearance occurs in aplastic anemia.

When radioiron citrate is deposited in the iron pool, a series of independent mechanisms operate for its removal. First, and most important, is hemoglobin synthesis (fig. 2). Loeffler and co-workers [5] have shown that iron citrate is rapidly bound to protein to become plasma iron. The plasma iron is subsequently picked up by the bone marrow, which converts it into hemoglobin. The hemoglobin in the red blood cells is discharged back into the blood stream. The cycle is complete when the red cells are destroyed in the spleen, and the liberated plasma iron is again available for hemoglobin synthesis.

A second pathway of iron removal is provided by the macrophages of the reticuloendothelial system in the liver, spleen, and bone marrow, which retain the iron as "iron stores."

The remaining pathways are the circulating reticulocytes which pick up a small amount of iron;[2a] iron used in the production of various metabolic enzymes; loss of minute amounts of iron in desquamated skin, sweat, and gastrointestinal mucosa; and, finally, the actual loss of iron which periodically occurs in the menstruating female (fig. 3, *left*). Iron returns to the circulation from three major routes: the hemoglobin cycle, the iron stores, and the exogenous iron absorbed through the gastrointestinal tract (fig. 3, *right*).

It should be stressed that the iron enters a "closed system." There is no physiological method for its excretion (excluding menstruation) other than the tiny amounts lost in desquamating skin or mucosal cells of the gastrointestinal tract.

All these pathways exist for and influence the plasma clearance rate of iron. A rapid clearing rate, therefore, simply indicates that one or more of these mechanisms is hyperactive. If all other mechanisms are normal, the clearance rate may be regarded as a direct index of the status of hematopoiesis.

The red blood cell uptake of iron eight days after its injection is a convenient double-check on the plasma clearance rate and represents a further study of the metabolic pathway for the iron that has been used by the marrow for hemoglobin synthesis. Except in three diseases, namely, pernicious anemia, Mediterranean anemia, and hemolytic anemia, fast plasma clearance rates are always associated with high red blood cell uptakes of iron and vice versa. In these diseases, extremely rapid plasma clearance times are the rule, indicating increased. erythropoiesis, but the red blood cell uptake does not always parallel these findings. The basis for the reliability of the use of clearance rate and red blood cell uptake as valid indexes of hematopoiesis is a series of classic experiments, both animal and human, and the clinical observations by various investigators, summarized by Huff and co-workers.[6]

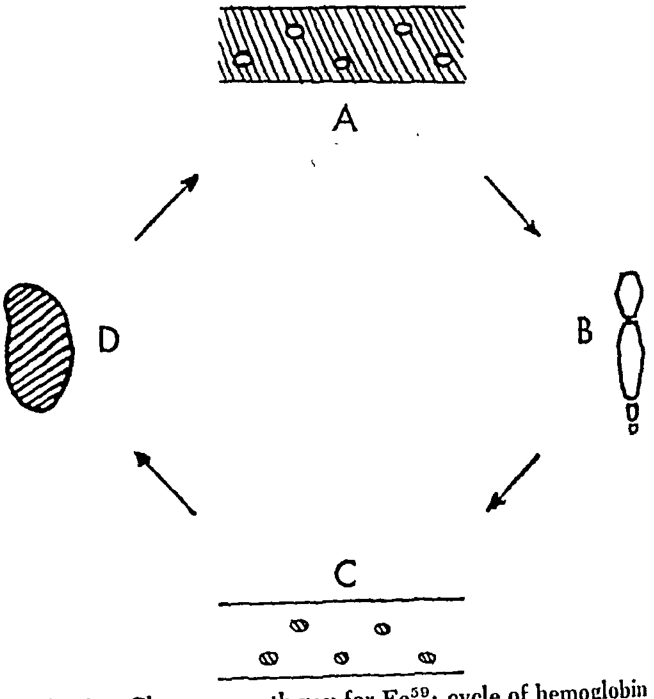

Fig. 2.—Clearance pathway for Fe^{59}: cycle of hemoglobin synthesis. *A*, circulating blood: formation of plasma iron; *B*, bone marrow: erythropoiesis; *C*, circulating blood: formation of red blood cell hemoglobin; *D*, spleen: destruction of red blood cells and liberation of plasma iron.

It is universally conceded that ionizing radiation in sufficient dosage will cause a loss of erythroid tissue of bone marrow. Hennessy and Huff[7] administered increasing doses of radiation to groups of rats and then performed radioiron cell uptake studies. They demonstrated a clear-cut, inverse relationship between the dose of irradiation given and the red blood cell uptake.

In studying patients with polycythemia vera before and after radioactive phosphorus (P^{32}) therapy, a well-defined relationship between the fast clearance rate in instances of untreated disease and the normal plasma clearance rate when the disease was in remission was observed. In addition, comparison of the plasma clearance rates of patients having polycythemia vera or secondary polycythemia with those of normal patients showed that both these disease states have associated rapid plasma clearance rates.[8]

In a series of patients with lymphoma who received nitrogen mustard, the depression of erythroid tissue was strikingly reflected in the delayed iron clearance time.[6]

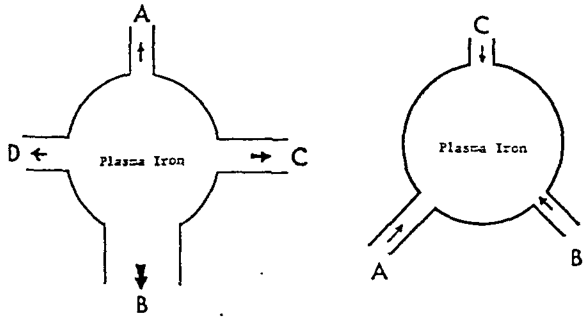

Fig. 3.—Interrelation of plasma pathways for Fe^{59}. *Left*, clearance pathways: *A*, reticulocyte uptake: production of metabolic enzymes, loss in desquamated skin, sweat, and mucosa; *B*, bone marrow: erythropoiesis; *C*, liver, spleen, and reticuloendothelial system: storage of iron; *D*, female uterus: menstruation. *Right*, renewal pathways: *A*, spleen: red blood cell destruction; *B*, liver, spleen, and reticuloendothelial system: storage of iron; *C*, gastrointestinal tract: absorption of exogenous iron.

The net gains in circulating red blood cell volume in sea level dwellers who move to higher altitudes is due to an increased rate of production of hemoglobin. A group of medical students in Lima, Peru, exhibited marked acceleration in iron clearance rates when they moved to a higher altitude. On the other hand, a slowing of this clearance rate was demonstrated in a group of Peruvian highlanders who moved to sea level.[9]

Finally, it is known that, when the product of a tissue or cell is supplied artificially, the producing tissue will often atrophy. Thus, a group of rats, given repeated transfusions that significantly elevated their hematocrit readings, demonstrated failure of their erythrocytes to utilize radioiron injected for red blood cell production, compared with control normals.[6]

In addition to the above data, the striking delay in iron clearance and low red blood cell uptake in patients with aplastic anemia has been repeatedly confirmed in every laboratory performing radioiron studies.

Thus, sound clinical, experimental, and theoretical bases exist for the use of radioiron as an indicator of hematopoiesis.

Objections to Radioiron Studies

One of the objections raised against radioiron studies is that it has been stated[10] that clearance rates and erythrocyte uptake are more directly related to the level of iron stores, and the level of plasma iron concentration, than to the status of hematopoiesis. That both iron stores and erythropoiesis influence the plasma clearance time and erythrocyte uptake is true. There are two clinical situations in which an actual error in interpretation will be made if plasma clearance and red blood cell uptake of iron are blindly considered to represent the status of erythropoiesis. In aplastic anemia, in which the iron stores are depleted with bleeding from the gastrointestinal tract or purpura, the plasma clearance time may be normal. This normal clearance time (when iron is cleared to add to the iron stores rather than for hemoglobin synthesis) can be erroneously interpreted as indicating adequate hematopoiesis. Contrariwise, the patient with hemochromatosis may be thought to have depressed erythropoiesis, when in fact the low erythrocyte uptake is solely due to the markedly diluted iron pool perfusing the bone marrow.

Beyond these two clinical situations the only errors that develop are those occurring when a quantitative estimation of erythropoiesis is attempted. In iron deficiency anemia, polycythemia, and after transfusions the degree of hematopoiesis may be overestimated. In iron deficiency anemias, rapid plasma clearance is due both to increased erythropoiesis and to the depleted iron stores; in polycythemia vera, after phlebotomies, rapid plasma clearance is due both to the increased erythropoiesis and to depressed iron stores. Whenever a transfusion is given, the iron clearance rate and the red blood cell uptake are depressed as a result of partial suppression of erythropoiesis and increase in iron stores.

Finally, when active bleeding occurs (from menstruation or other causes), the plasma clearance rate will be rapid and the erythrocyte uptake will be elevated, independent of erythropoiesis and the level of the iron stores. Theoretically, blood loss may be estimated in this fashion if the iron stores and erythropoiesis remain constant during the period of study.

The obvious factor that emerges is that radioiron studies, like all tests in medicine, require intelligent interpretation. Direct application should not be made without clinical knowledge of the case. An analogy exists between radioiron and radioiodine studies. The 24-hour radioactive iodine uptake of the thyroid gland is an accurate index of hyperthyroidism, assuming that the patient's iodine pool is not contracted, i. e., that the patient is not "iodine starved," and that the rapid uptake by the thyroid gland is not an effort to produce an adequate amount of thyroid hormone from a depleted iodine pool.

A second argument[11] raised against radioiron studies is that they fail to supply information that could be otherwise obtained. Until the advent of the use of radioisotopes, erythropoiesis could be gauged solely by the numbers of reticulocytes in the peripheral blood. Though reticulocytosis (increase in the number of circulating reticulocytes) is a rather reliable index, its accuracy is directly proportional to the skill of the examiner. For instance, values ranging from 1.4 to 4.7% on the same blood specimens were reported by different technicians in the Bellevue Hospital laboratory. The assessment of relative degrees of reticulocytopenia is highly inaccurate because of the great number of cells which must be counted. Realizing how much reliance is placed on this single test, the need for an additional objective measure of erythropoiesis (especially arrested erythropoiesis) is apparent. Even a bone marrow study supplies information about only the status of the microscopic fragment of tissue under study. Spotty destruction of bone marrow and extramedullary erythropoiesis minimize the value of the bone marrow study as an index of the general status of erythropoiesis. Bone marrow study has the additional drawback of requiring a sternal puncture.

Beyond its ability to correlate with erythropoiesis, one other facet is unique to the injected tracer-iron study: it gives clear, unequivocal information about the dynamic status of newly injected iron. The test shows what percentage of the iron is incorporated into the red blood cells and how rapidly it is cleared out of the blood. Today, with increasing use of parenterally injected iron, the question of iatrogenic hemochromatosis has been raised. Some hematologists have suggested that a sternal puncture of the marrow be stained for iron, or that plasma iron studies be performed, and that parenterally given iron therapy be withheld if any significant indication of increased iron stores is found.[12] A direct test is to determine how rapidly radioactive iron clears out of the blood stream. If there is delayed plasma clearance, either as a result of saturated iron stores or even as a result of aplastic anemia, parenteral administration of iron would not appear indicated. This simple test represents a unique contribution of tracer iron studies: a method to control the use of parenterally administered iron.

A third objection raised to radioiron studies is that they involve a radiation hazard. Iron 59 (Fe^{59}), whose physical half life is 45 days, emits in its decay beta particles of 0.3, 0.4, and 1.6 Mev, and gamma rays of 1.1 and 1.3 Mev energies. The maximal permissible weekly dose of 0.3 r will be delivered to the whole body of a "standard man" by 13 μc of Fe^{59}. Since less than 5 μc are used in this study, a "standard man" received a dose of less than 0.12 r weekly, well below the accepted level for continuous exposure of occupational workers, without even considering the diminution in dose resulting from physical decay.

A fourth objection raised to radioiron tests is that they are difficult to perform and that results are not easily reproducible in different laboratories. The argument has lost its validity since we have introduced simplifications in the technique.

Simplifications in Technique

Use of 4 μc of Ferrous Citrate Injected Intravenously as Tracer Dose.—In the past, different investigators have used ferric beta-globulinate and ferric chloride in large amounts as the tracer dose. The use of different tracer materials, and varying tracer doses, has caused the failure of reproducibility of results in various clinics. It has been shown[13] that the red blood cell uptake in monkeys is significantly different if ferric chloride is substituted for ferrous citrate. Further, extremely large doses of Fe^{59} altered the size of the iron pool and therefore invalidated comparisons with studies in which smaller doses were used. It is important, therefore, to use a standard dose of a standard Fe^{59} preparation. We have selected ferrous citrate, which has been shown to be rapidly bound to the iron-binding fraction of the blood after intravenous administration,[5] because it is the simplest to handle. Both ferric beta-globulinate and ferric chloride must first be incubated with a sample of the patient's blood before injection; ferrous citrate, on the other hand, may be directly injected intravenously. The approximate dose of 4 μc was selected, because it supplies good counting statistics, gives an insignificant amount of radiation to the patient, and does not alter the iron pool.

Performance of Plasma Clearance on Whole Blood Instead of Plasma.—Early in our studies clearance studies were done on both whole blood and plasma. When it was verified that there was no difference between the results obtained with these determinations, plasma counting was abandoned and only whole blood specimens were counted. This simplification eliminates the need for centrifugation in the determination of the plasma clearance rate. It further eliminates the need for obtaining the hematocrit reading in determining the eight-day red blood cell uptake (see step 9 under "technique").

Reporting of Plasma Turnover Data as One-half Time Rather Than as Milligram of Iron Cleared per Unit Time.—Hematologists[14] originally reported all their iron studies as plasma iron turnover rates rather than as plasma clearance one-half time. The turnover rate is calculated from the following formula:

(plasma iron turnover rate) = ([serum iron concentration] ÷ [1.4 × plasma clearance half time])

The serum iron concentration is an essential component of the formula, and its determination is too difficult for routine performance in the average clinical or radioisotope laboratory. The difficulty inherent in this test has tended to discourage some laboratories from undertaking ferrodynamic studies. It is, in fact, questionable whether a combination of laboratory data is as valuable as single determinations considered separately. The serum iron concentration has no connection with ferrodynamic studies, and, while useful information may be obtained from it, it is not an essential part of radioiron studies.

Performance of a Single Eight-day Red Blood Cell Uptake.—Reference to figure 4 clearly illustrates that at eight days the red blood cell uptake in cases of aplastic anemia is sharply separated from that in all other anemias associated with an active bone marrow. This finding has been amply confirmed in our laboratory and in all reports in the literature. Pernicious anemia, Mediterranean anemia, and certain cases of hemolytic anemia do not fall into this pattern.[7] In cases of pernicious anemia and Mediterranean anemia the curves are gradually rising, without plateaus. Certain cases of hemolytic anemia present biphasic changes, others are characterized by low erythrocyte uptakes, and still others by high uptakes. In all other enemias with an active bone marrow, there is a specific pattern characterized by a plateau after the seventh day of red blood cell uptake. The performance of daily tests up to 14 days to obtain a curve of red blood cell uptake is an excellent experimental method; it is not, however, practical as an everyday clinical test. Determination of a single eight-day red blood cell uptake yields adequate information about the status of hematopoiesis in most anemias, requires a single return visit on the part of the patient, and a single determination. It is the preferred method for everyday clinical use.

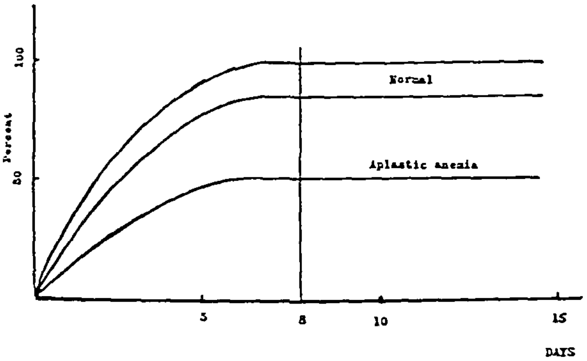

Fig. 4.—Red blood cell utilization of plasma Fe^{59} after intravenous injection. In aplastic anemia, uptake by red blood cell fraction is significantly depressed. At eight days, difference between curves in aplastic anemia and normality is clear-cut.

Modification of Technique of Red Blood Cell Uptake.—The red blood cell uptake, as originally performed and described in the literature, was complex and technically difficult to perform. It required accurate counting of the sample of radioactivity introduced, the nomographic estimation of the blood volume, and the counting of packed red blood cells. A 5 to 10% error is inherent in the accurate counting of any sample of radioactivity introduced into the blood stream. The use of nomograms to determine whole-blood volume on the basis of height and weight leads to a considerable error, because these nomograms fail to consider the sex, age, habitus, and clinical condition of the patient (e. g., a state of hydration). Counting packed red blood cells necessitated (1) a hematocrit determination, (2) a calculation of the specific amount of blood required to yield 1 cc. of packed cells by centrifugation, and (3) the actual counting of this volume of red cells. It became obvious, therefore, that the original, complicated and long red blood cell uptake determination had to be simplified if it was to be introduced as an everyday laboratory procedure, and if comparable results were to be obtained by different laboratories. Accordingly, the following mathematical exercise was performed:

In the basic formula for red blood cell uptake,

(Counts/cc. packed RBC × RBC volume) ÷ (counts injected) × 100

when

(counts/cc. whole blood) ÷ (hematocrit)

was substituted for counts per cubic centimeter of packed red blood cells, and hematocrit multiplied by blood volume was substituted for red blood cell volume, and

(counts injected) ÷ (counts/cc. whole blood at time zero)

was substituted for blood volume, the formula became:

([counts/cc. whole blood] ÷ [hematocrit]) × (hematocrit) × ([counts injected] ÷ [counts/cc. whole-blood time zero]) ÷ (counts injected)

which simplifies to:

(counts/cc. whole blood) ÷ (counts/cc. whole-blood time zero)

Hence, this test requires the counting of whole-blood samples. The entire test, therefore, is reduced to counting whole-blood samples at given intervals up to 120 minutes, followed by the counting of a whole-blood sample at eight days.

We found justification for substituting

(counts/cc. whole blood) ÷ (hematocrit)

for counts per cubic centimeter of red blood cells after performing many determinations on whole blood and plasma at the eighth day and constantly finding no activity in the plasma. A correction can, however, be applied if activity is found (see step 10 under "technique").

Two tables are presented below. Table 1 indicates the clinical situations in which radioiron tracer studies provide useful clinical information which can be directly applied in the management of patients. Table 2 indicates the radioiron tracer data in other hematological conditions, which data are of solely academic interest today.

TABLE 1.—*Conditions in Which Ferrodynamic Studies Provide Important Information Directly Applicable to Management of Patients*

Condition	Type of Study: ½-Time Clearance, Min.	Type of Study: 8-Day Red Blood Cell Uptake, %	Clinical Application
Normal	65-115	100	...
Aplastic anemia	Over 120	Below 70	Controls' use of marrow depressants: x-rays, nitrogen mustard, chlorambucil, or busulfan produce aplastic anemia discoverable long before changes in peripheral blood.
Iron deficiency anemia	Under 60	100	Controls' use of parenterally given iron: when one-half time is normal, further parenteral administration of iron should be questioned.
Leukemia	Variable	Variable	In leukemia, anemia may be due to either encroachment on marrow, aplastic anemia secondary to treatment, or hemolysis: when aplastic anemia develops, further therapy with x-rays or other marrow depressants is contraindicated.[15]
Polycythemia vera	Under 60	100	Controls' use of P^{32}: when disease is under control, one-half time is normal; when one-half time is accelerated, re-treatment is indicated.

TABLE 2.—*Conditions in Which Ferrodynamic Studies Provide Information Solely of Academic Interest*

Condition	Type of Study: ½-Time Clearance, Min.	Type of Study: 8-Day Red Blood Cell Uptake, %	Interpretation
Normal	65-120	100	...
Hemochromatosis	40-70	Low	Slightly delayed one-half time and low 8-day red blood cell uptake are related to saturated iron stores rather than to arrested erythropoiesis.
Blood loss anemia	Under 50	100	Accelerated half-time and high red blood cell uptake are reflections both of depleted iron stores and stimulated erythropoiesis.
Hemolytic anemia	Under 60	Erratic	Hemolytic anemia provides confusing information when studied by 8-day red blood cell uptake. In all cases here reported, uptakes near 100% were obtained. However, in the literature cases are described in which uptake is low, and others in which a biphasic curve is obtained. To be properly studied, a complete daily uptake measurement is necessary. This ceases to be a simple clinical test.
Pernicious anemia	Under 60	Meaningless	In these two disease entities, the 8-day red blood cell uptake is meaningless because there is no plateau in the uptake curve after 7 days, but simply a steadily rising curve. To be properly studied, a complete daily uptake measurement is necessary. This ceases to be a simple clinical test.
Mediterranean anemia	Under 60	Meaningless	

Summary and Conclusions

The method of performing radioiron tracer studies, as performed in the Radio Isotope Laboratory of Bellevue Hospital, is as follows: After intravenous injection of about 5 μc of radioactive iron (Fe^{59}) citrate, whole blood samples are taken at 5, 15, 30, 60, 90, and 120-minute and eight-day intervals. By directly counting 4 cc. aliquots, the plasma clearance one-half time and the eight-day red blood cell uptake are obtained. The normal plasma clearance one-half time is 65 to 110 minutes; the eight-day red blood cell uptake (RBCU) is 85 to 100%.

The justification for interpreting these tests as indexes of erythropoiesis have been reviewed, and objections to the use of the test have been challenged. Two tables summarize the clinical usefulness of radioiron studies.

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INTRASYNOVIAL INSTILLATION OF TRIAMCINOLONE ACETONIDE

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The intrasynovial injection of triamcinolone acetonide for the relief of arthritic or bursitic pain was carried out in 67 patients. They were selected because of pain, tenderness, or limitation of motion, occurring primarily in a single joint or bursa. The injections were into a joint cavity in 25 patients and into a bursa in 42. The usual dose was 5 mg., with a volume of 1 ml. Aseptic techniques were strictly observed, and no infections occurred. The results were good to excellent in most cases; swelling and pain were reduced, and mobility was increased. The dosage of triamcinolone acetonide used did not cause untoward side-effects, either local or systemic, even when repeated twice weekly for several months.

The intrasynovial instillation of corticosteroids is a practical and often strikingly successful palliative treatment for active rheumatoid or arthritic involvement of peripheral joints when inflammation and pain are essentially confined to one or two and when widespread migration of the disease process has not occurred.[1] When a response is elicited, benefits are prompt if only temporary. Initially, there is lessening of stiffness, articular tenderness, and pain followed by a subsidence of swelling and an increase in range of motion. This is achieved with considerably less risk of the physiological disturbances associated with oral dosage of the same compound, even though effects are transient and repeated injections may be required. In customary doses, which can be absorbed by the synovium, the locally instilled corticosteroid does not have any appreciable systemic effect.[2] Series of injections have been given at regular intervals without untoward reactions.[3]

Intrasynovial instillation is a relatively simple procedure, mastered without too much difficulty in the limitations of office or outpatient facilities. The primary contraindication is the presence of infection in adjacent supporting tissues. The important precaution is a strict application of aseptic techniques. Observation of this principle will largely avert the chance introduction of infection into the joint itself. A joint infection rate of less than 1 in 4,000 has been reported for more than 17,000 injections.[14] Fundamentally, the hazards of mechanically placing a corticosteroid within a joint space are the same as with any other paracentesis or with a lumbar puncture, and the same meticulous care must be observed.

Full details of the actual technique of intra-articular or intrasynovial injection are available. The skin is cleansed as thoroughly as possible. The area is sprayed with ethyl chloride or infiltrated with procaine to guard against pain on insertion of the needle. Because the synovial pouch is nearest the skin on extensor surfaces, this approach to the affected joint is most convenient. A knowledge of joint architecture is desirable, and a clear diagram is a suitable guide to the proper positioning of the needle. A 20-gauge or smaller size needle is rapidly inserted into the joint cavity with less pressure required to advance the needle once the joint capsule is entered. Injection of a small amount of air is possible if the needle is in position. Otherwise, pressure on the plunger of the syringe will meet with resistance, or actual rebound may occur. When it is certain that the needle is properly in place, the corticosteroid suspension is injected. After the treatment, a sterile dressing or supportive elastic bandage is applied.

Corticosteroids such as cortisone, hydrocortisone, prednisone, and prednisolone, used systemically in the treatment of rheumatoid and arthritic disease, have been applied locally; hydrocortisone is the most widely used agent for direct instillation. Since the synovium can absorb only limited quantities of active material and as joint size qualifies the amount of suspension which can be introduced, the potency of the corticosteroid is an important influence on the success of treatment. This is particularly true in severely inflamed joints where a significantly greater suppressive action must be present for patient benefits. Triamcinolone acetonide (Kenalog), a recent development in corticosteroid research, exerts a pronounced local anti-inflammatory effect after being given in low dosage. A suspension containing 10 mg. of triamcinolone acetonide per milliliter has been prepared for intrasynovial instillation and for parenteral use. The suspension was used in the treatment of inflammatory joint involvement in a series of patients encountered in office practice.

Distribution of Joint Involvement and Response to Local Therapy With Triamcinolone Acetonide

Condition Treated	Patients, No.	Symptomatic Improvement			
		Excellent	Good	Fair	Poor
Arthritis					
Hands and fingers	4	3	1	0	0
Ankles, feet, and toes	5	5	0	0	0
Acromioclavicular	2	0	2	0	0
Shoulder	1	1	0	0	0
Sacroiliac	3	1	2	0	0
Hip	5	1	3	1	0
Knee	5	0	5	0	0
Bursitis					
Shoulder	6	3	3	0	0
Subdeltoid	12	11	1	0	0
Elbow	3	2	1	0	0
Wrist	4	3	1	0	0
Trochanter	7	2	5	0	0
Ischial tuberosity	1	0	1	0	0
Knee	9	5	4	0	0
Totals	67	37	29	1	0

Clinical Material

A group of 67 patients selected because of prominent symptoms of swelling, pain, tenderness, and limitation of motion occurring primarily in a single joint or bursa were given triamcinolone acetonide intra-articularly during this study. Eighteen men and 49 women, ranging in age from 19 to 85 years (the greater number in their fifth or sixth decade) showed a fair to good general physical condition. Diagnoses included rheumatoid and degenerative osteoarthritis with various joint involvements and traumatic or inflammatory bursitis chiefly affecting knee, elbow, subdeltoid, and shoulder. The distribution of joints treated is presented in the table.

Duration of symptoms extended from one day to several years. Forty-three patients reported difficulties present six months or less; 24 experienced joint symptoms for two or more years. Decompensated back in two patients, trauma in one, advanced arthritides in five, and age in one were co-existent or complicating factors requiring active treatment. Twenty-three patients received adjunctively multivitamins, physiotherapy, antibiotics, and orally given corticosteroids; one person received instillation of novocaine. Of the 67 patients in this series, 27 had previously been treated with instillations of hydrocortisone and some with novocaine as well.

Triamcinolone acetonide was injected in doses of 2.5 to 10 mg. (0.25 to 1.0 ml.); the smaller dosages were given in bursae and hand joints. The usual dose was 5 mg. (0.5 ml.). Seven patients required only one injection for symptom control. In the remaining patients, frequency of instillation ranged from twice weekly to twice monthly, with 35 in treatment for three months or less and 25 for three to six months. All patients were ambulant.

Therapeutic Results

Triamcinolone acetonide given intra-articularly proved to be a potent anti-inflammatory agent. The results of treatment were good to excellent in most of the patients presented here (see table). Response was graded according to reduction in swelling and pain, increase in mobility, and duration of effect as well as subjective experience of subsidence of the acute symptoms. Most patients previously given intra-articular injections of hydrocortisone noted a better response with triamcinolone acetonide. In one patient, benefits attributed to triamcinolone acetonide were considered only fair because of a shorter duration of anti-inflammatory action than observed with hydrocortisone at the dosage level used. In all patients, however, improvement with triamcinolone acetonide was achieved with considerably lower dosage than necessary when hydrocortisone was instilled. As far as could be determined, no lessening of effect resulted after repeated injections.

No evidence of local toxicity and no systemic corticosteroid effects occurred in this series during a maximum treatment period of six months. Although three patients experienced upper respiratory infections and two of these also developed ethmoiditis while undergoing treatment, no adverse influence on the ultimate course of the disorders was detected.

Comment

Remission of inflammation, pain, swelling, and stiffness usually occurs within 48 hours of direct instillation of a potent corticosteroid into the joint cavity. Intrasynovial therapy is an effective but temporary measure for producing palliative anti-inflammatory action where one or two joints are more severely involved or where systemic corticosteroid therapy is contraindicated. Repeated injections may be given without serious hazard to the patient, since customary doses are absorbed by the synovium and systemic influences are of no appreciable consequence. The potency of the corticosteroid used is an important consideration affecting the outcome of treatment, particularly in severely inflamed joints, as the synovium can absorb only limited quantities of the drug, and the actual amount of active agent which can be introduced is determined by the size of the joint. Experience with triamcinolone acetonide indicates that it is a highly potent anti-inflammatory substance for intrasynovial use, relieving joint symptoms in an exceptionally high percentage of the patients treated. Improvement was achieved with considerably lower dosage than necessary with hydrocortisone. Enhanced potency is apparently unaccompanied by an increased propensity for producing toxic reactions or by evidence of systemic influences.

Summary

Intrasynovial instillation of triamcinolone acetonide (Kenolog) accomplished good to excellent symptomatic improvement in 66 of 67 (98.5%) patients with rheumatoid and arthritic disorders affecting peripheral joints. Benefits were manifested by a sharp reduction in stiffness, tenderness, and pain; by a subsidence of swelling; and by an increase in joint mobility.

Most patients noted a better response to triamcinolone acetonide than to hydrocortisone, and this was achieved with considerably lower dosage. Injections of 2.5 to 10 mg. were given with a frequency ranging from twice weekly to twice monthly for periods up to six months in duration. All patients remained ambulant. No evidence of local toxicity and no systemic corticosteroid influences were observed in this series. This experience indicates that triamcinolone acetonide is a highly active anti-inflammatory agent for direct instillation into the joint cavity.

720 N. Michigan Ave. (11).

The triamcinolone acetonide used in this study was supplied as Kenalog through the courtesy of Dr. R. C. Merrill, E. R. Squibb & Sons, New York.

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MOBILITY OF THE NORMAL SPINAL CORD.—The position of the cervical spinal cord is not constant and it changes in the antero-posterior direction. These differences which are dependent on the position of the body can reach in the normal 9 mm. The movements of the spinal cord are different at various levels and the mutual relation of these differences is relatively constant, the minimal shift being at the level of the third cervical vertebra. From this segment cranially and especially caudally the mobility of the spinal cord increases. . . . The degree of mobility of the spinal cord has no relation to the antero-posterior diameter of the normal spinal canal. The values of the movements of the spinal cord are higher in the lower and narrower part of the cervical spinal canal than in the upper and wider part of it. Changes of shape of the spine, i. e. anteflexion and retroflexion, have a certain, but by no means decisive influence on the relations between the spinal cord and the walls of the spinal canal. Key and Retzius wrote in 1875: "In the prone position of the cadaver the spinal cord shifts forward and in the supine position backwards. Probably similar conditions are also during life." Our present pneumomyelographic studies in the living confirmed these anatomical conceptions of the Swedish authors.—J. Jirout, M.D., The Mobility of the Cervical Spinal Cord Under Normal Conditions, *The British Journal of Radiology*, November, 1959.

SWEAT GLAND CARCINOMA WITH METASTASES

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Sweat gland carcinomas with distant metastases have been infrequently recorded in the literature, the first case being reported by Hedinger [1] in 1911. Most of these tumors have originated in areas where the apocrine sweat glands are located. Primary tumors of the hand are also uncommon; of 750,827 patients seen at the Henry Ford Hospital and Clinics the incidence of primary hand tumors was 0.008%.[2] While Schreiner and Wehr [3] found an incidence of 1.1% in their series, no sweat gland tumors were present in either series. The rare combination of a sweat gland carcinoma located in a nonapocrine sweat gland–containing area, a finger, associated with distant metastases justifies this report.

Gates and co-workers [4] reviewed the world literature from 1865, when the first case of sweat gland carcinoma was recorded, to 1939. They found 29 cases of sweat gland carcinoma, but in only four instances had metastases occurred. A diagnosis of carcinoma was made in the other cases on the basis of local invasion and cellular anaplasia. Stout and Cooley [5] accepted seven cases of metastasizing sweat gland carcinoma in their review of the world literature and added six of their own. In 1956, Smith [6] added the first case to the British literature and acknowledged 20 of those contained in the entire literature. Kay and Hall [7] and Elliott and Ramsay [8] each reported a case, and the present case report brings the total cases of sweat gland carcinoma with distant metastases to 24.

Report of a Case

A 62-year-old man had been unable for 18 months to extend completely the ring finger of his right hand without pain. He had noted a resistance to extension of his finger at 130 degrees; with some effort the finger could be extended, with a resulting audible snap. He had been aware of a slowly growing lump in his right palm for the last eight years. In 1946, he caught the little finger of his right hand in a car door, and the severe crushing injury necessitated amputation at the proximal interphalangeal joint. After his surgeon reported that a sweat gland carcinoma was found in the surgical specimen, he remembered having a small, hard movable nodule at his proximal interphalangeal joint for many years. No more definitive treatment was done because it was believed that the tumor had been removed completely.

Physical examination on admission revealed a grossly normal right hand, minus the distal an middle phalanges of the fifth finger. There was a nontender movable 1.5-cm. mass in the right palm This mass appeared attached to the deep structure beneath the skin of the palm at the distal creas overlying the head of the fourth metacarpal. Th skin moved freely over the mass. No limitation o motion was present except in the ring finger of th right hand. A resistance was felt at 130 degrees o flexing the metacarpophalangeal joint, which, o slight exertion and accompanied by an audible snap could be fully extended. There were several small hard nodules in the right axilla. The rest of th physical examination was essentially noncontributory. Laboratory studies, including blood cell count urinalysis, and determination of levels of blood calcium, phosphorus, and alkaline phosphatase, gave normal results. Roentgenograms made of the chest, hand, and skeleton showed no metastatic disease.

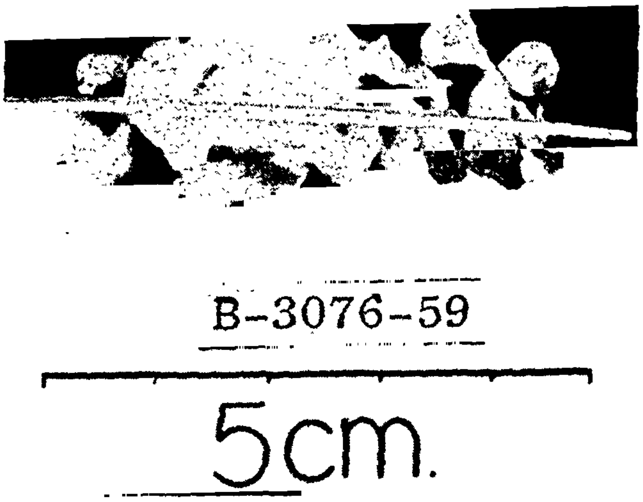

Fig. 1.—Tumor in sagittal section; toothpick lying in tendon sheath, which was encircled by tumor.

Exploration of the right palm, on July 20, 1959, revealed a hard, gritty, yellow-white tumor which enveloped the profundus and sublimus tendons of the right finger. It was not encapsulated and on gross examination did not appear to invade the adjacent muscles. The tumor extended from the proximal flexor sheath to just short of the transverse carpal ligament. The tumor was thought to have been completely removed grossly. It weighed 5 Gm. and measured 5.0 by 0.5 by 1.0 cm. On Aug. 3, 1959, several hard, matted nodes were removed from the right axilla. On cut section examination, these nodes were grossly tumorous.

From the departments of pathology and orthopedic surgery, Wadsworth Hospital, Veterans Administration Center.

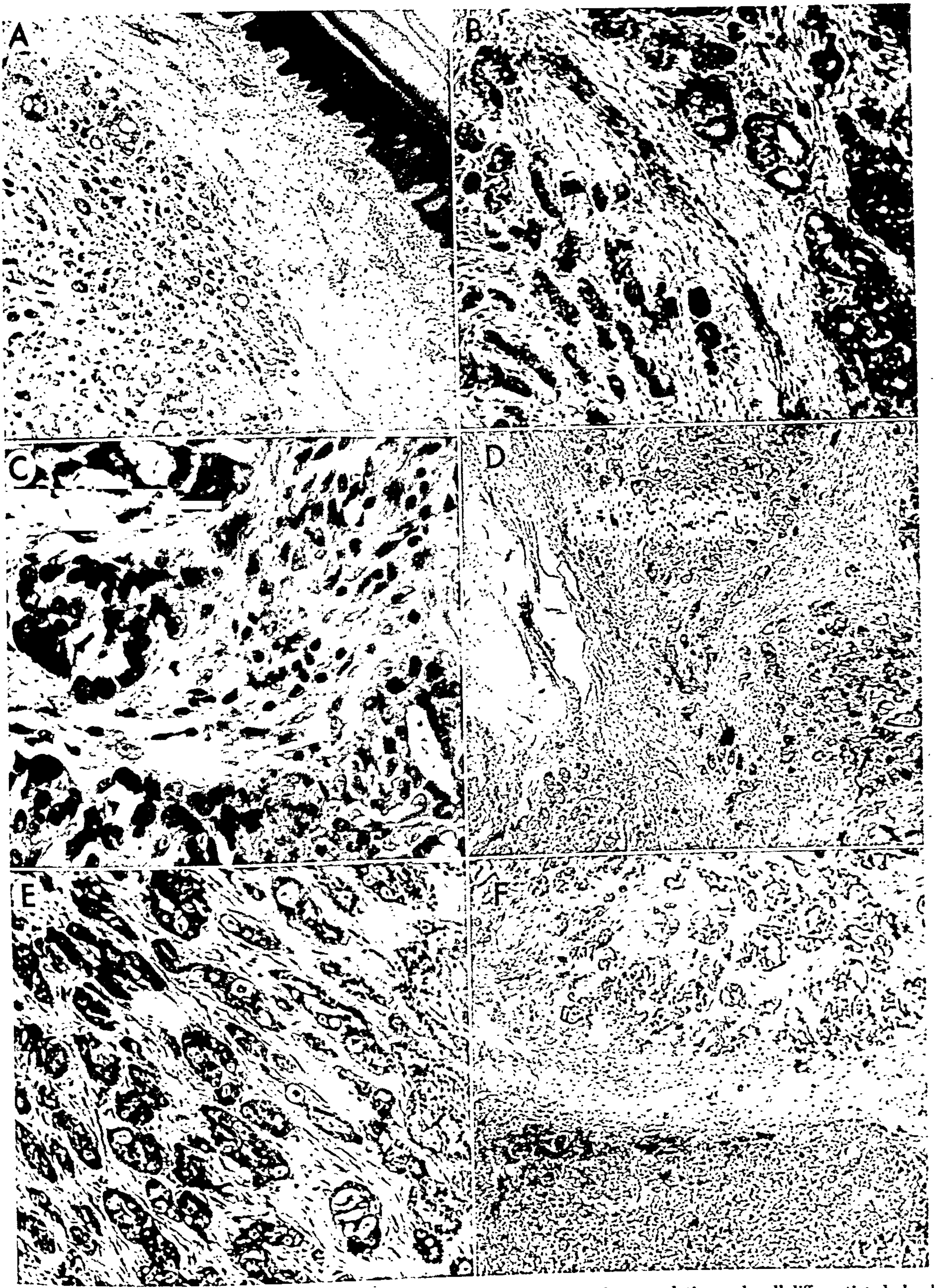

Fig. 2.—(*A*), primary adenocarcinoma of sweat gland origin, showing lack of encapsulation and well-differentiated glandular pattern (× 35); (*B*), high-power view reveals fibrous bands isolating tumor cells, which show acinar formation (× 100); (*C*), pleomorphic and anaplastic character of tumor cells (× 430); (*D*), metastatic tumor infiltrating profundus tendon. Tumor retains microscopic characteristics of primary (× 35); (*E*), metastatic tumor in palm at higher magnification (× 100); (*F*), metastatic tumor to axillary node retaining microscopic characteristics of primary (× 35).

The original slides from 1946 were obtained and reviewed; these showed adenocarcinoma of sweat gland origin. Microscopic review of tissue removed from the axilla and palm showed an identical cellular pattern. Results of mucin precipitation tests of the palmar tissue revealed mucin within the glands. Amputation through the forearm, accompanied by an axillary dissection, was advised but refused by the patient. At the time of writing, three months after excision, the tumor has shown no further extension.

Comment

Sweat gland carcinomas originate in the skin in areas where apocrine sweat glands normally occur, such as the axillary region, vulva, and scrotum, but they may arise elsewhere in the skin. They afflict the older age group predominantly and have an equal sex incidence. The presence of these tumors in the latent state is usually known to the patient for a long time, as long as 35 years in some cases. The true, aggressive nature of the tumor is disclosed by its increase in size. These tumors are characterized by red or violet firm elevated nodules or nodules that are fixed to the underlying and adjacent skin. They must be differentiated from dermatofibrosarcoma protuberans, keloid, metastatic carcinoma, and lymphosarcoma of the skin which also show characteristically red-violet nodules.

These neoplasms have proved to be radioresistant and consequently the therapy must be exclusively surgical. Management must be based on the clinical extent of involvement and the knowledge that sweat gland carcinoma has an aggressive infiltrative capacity. A generous surgical excision for clearance and histological examination should be undertaken. If histological clearance has not been obtained under the original excision, wider excision and skin grafting, if necessary, should be performed. Ablation of the affected area is justified when clearance of the tumor is questionable. If local skeletal involvement has occurred, amputation is necessary. The presence of involved regional lymph nodes requires a radical dissection of the region.

Summary

The rare combination of a sweat gland carcinoma of the finger with distant metastases occurred after a latent period of 13 years. This is the first time that this combination has been reported.

5100 W. 116th St. (45).

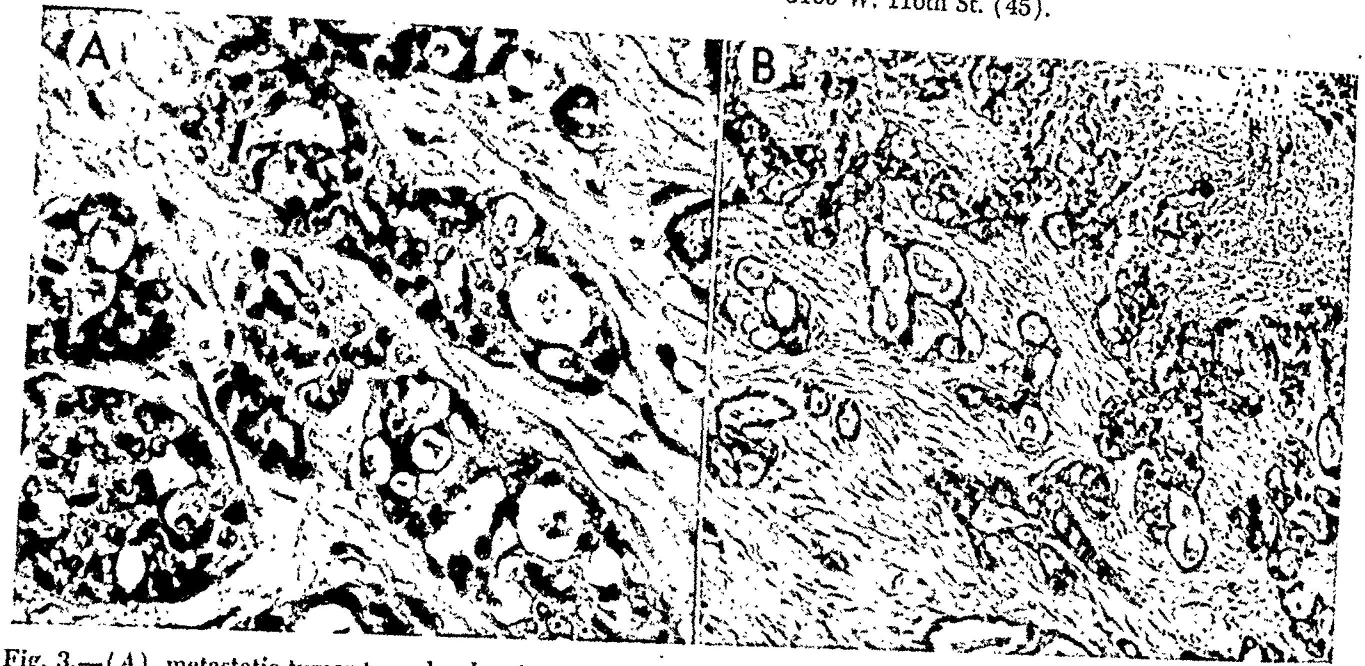

Fig. 3.—(*A*), metastatic tumor to node, showing nest of cells in gland formation with mucous secretion, as seen also in palm and finger slides (× 100). (*B*), metastatic tumor with node showing gland formation, as in other sites above (× 430).

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EXERTION-INDUCED MYOGLOBINURIA AND HEMOGLOBINURIA

SIMULATION OF ACUTE GLOMERULONEPHRITIS

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Extensive repetitive calisthenics performed by Marine recruits were followed by swelling of the quadriceps muscles, dark urine, albuminuria, hematuria, pyuria, red blood cell casts, myoglobinuria, and hemoglobinuria. In all 19 patients who were hospitalized albuminuria was demonstrable. Spectrophotometric and chemical study of dark urine specimens from these persons revealed excretion of both myoglobin and hemoglobin. Renal biopsy specimens of two patients, one of whom experienced acute renal failure, disclosed tubular abnormalities compatible with acute tubular necrosis. After recovery, resumption of the same calisthenics did not cause reappearance of renal or muscular symptoms.

For several years physicians at the U. S. Navy Hospital, Beaufort, S. C., have been aware of a peculiar syndrome occurring after excessive performance of a calisthenic known as the "squat jump" (fig. 1). After performance of squat jumps, some recruits developed myoglobinuria, hemoglobinuria, albuminuria, hematuria, and urinary casts. The initial clinical findings sometimes closely resembled those of acute glomerulonephritis.

This calisthenic consists of a jump into the air from a squatting position, so that the body weight is shifted from one leg to the other. Maximum strain thus is placed on alternate quadriceps muscles during the jump. This calisthenic was usually repeated many times in a rapid manner. It is extremely difficult for even a well-conditioned person to perform more than 80 squat jumps in succession.

Nearly all recruits were troubled by marked stiffness of the quadriceps muscle when squat jumps were first performed. About 60 recruits of 28,000 (0.21%), during the year 1958, sought medical care because of difficulty in walking or passage of dark urine.[1] Of these 60 recruits, 12 were hospitalized because of the severe pain and swelling of the muscle or the persistence of urinary abnormalities beyond a two-day observation period in a dispensary. The true incidence of squat jump syndrome was impossible to ascertain, because well-motivated recruits frequently do not seek medical care.

The squat jump syndrome consisted of the passage of dark urine in association with painful swelling and induration of the quadriceps muscles. The typical case developed within a few days after the initial performance of daily squat jumps. No pain or swelling of muscle was ever noted during the performance of squat jumps. The swelling and pain of the quadriceps characteristically began in the evening, four to six hours after completion of the exercise, and always preceded, or was concurrent with, the passage of dark urine. The severe swelling of the quadriceps gradually decreased in the first three or four days and was rarely evident longer than one week. No muscle atrophy or weakness followed recovery. Passage of dark urine often was of transient duration, although it persisted as long as 96 hours in some patients.

Patients with squat jump syndrome exhibited various urinary abnormalities including myoglobinuria, hemoglobinuria, albuminuria, hematuria, pyuria, granular casts, and red blood cell casts. Albuminuria, which occurred consistently in this syndrome, was maximal during the period when the urine was dark. Within three or four days after the onset of symptoms, urinalysis was normal in all but four patients.

The squat jump syndrome was first regarded as a completely benign condition. Those patients hospitalized were allowed to be ambulant as soon as their muscle swelling and pain had disappeared and were returned to duty when a normal urinalysis was obtained. The patient in case 15 (table 1) was the first observed whose illness did not fit the pattern of a benign condition. This case and five others of exertional myoglobinuria will be reported in detail. Urinary findings in the remainder of cases are listed in table 1. The data for cases 1 through 5 were obtained from the 1957 records of the U. S. Navy Hospital, Beaufort, S. C. Cases 6 through 19 were observed personally.

Myoglobin in the urine was demonstrated by the method of Blondheim and co-workers.[2] Spectrophotometric studies of the urinary pigments were performed by Dr. Richard H. Gadsden[3] of the Chemistry Department of the Medical College of South Carolina; a Beckman DK-2 spectrophoto-

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meter was used. Urine supernatants were tested for occult blood by the use of orthotolidine (Hematest) reaction tablets. The Wallace-Diamond qualitative test was used for urinary urobilinogen determination.

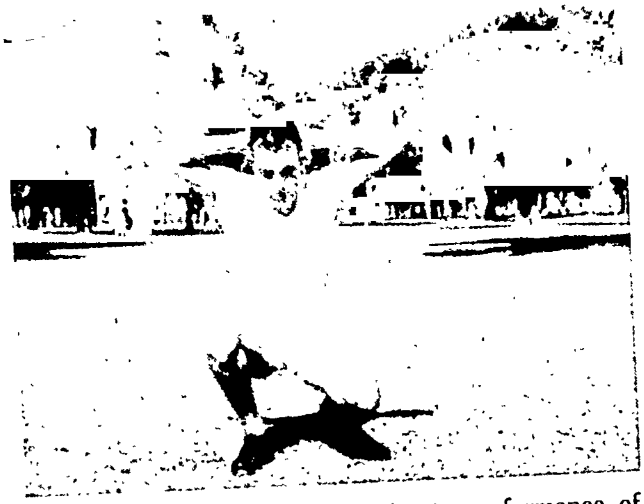

Fig. 1.—Position assumed prior to performance of squat jump.

Report of Cases

Case 1.—An 18-year-old recruit noted passage of red urine and pain in the quadriceps muscles after three days of training, which included squat jumps. He was unable to recall having had any recent upper respiratory infection. Physical examination disclosed tenderness of the lower rectus abdominis and of both quadriceps muscles. Urinalysis revealed a 345-mg.% level of protein and many red blood cells per high-power field. The supernatant gave a strongly positive reaction for occult blood.

The patient was kept at bed rest for two months. Despite this, the urine continued to exhibit a protein level of 20 to 100 mg.% and slight microscopic hematuria for seven months. An intravenous pyelogram disclosed no abnormalities. Throat cultures and serum antistreptolysin O (ASO) titers were not obtained. The patient was discharged from the Marine Corps with a presumptive diagnosis of subacute glomerulonephritis.

Case 15.—A 20-year-old recruit performed 35 squat jumps. The next day he became weak, nauseated, and complained of fever and chills. He continued to perform daily squat jumps, and on the fourth day was found to have a temperature of 104 F (40 C). The pulse rate was 128 per minute and the blood pressure 100/70 mm. Hg. The patient seemed to be mentally confused and was treated for heat stroke with a whole-body ice pack. The next day he complained of tightness in both quadriceps muscles, which were swollen and tender to pressure. On the same day he began to have oliguria, and the urine was noted to be dark brown in color. On the fifth day of illness his blood pressure had risen to 140/98 mm. Hg.

On the third day of his illness, the urine contained 500 mg.% of protein and innumerable red blood cells with red blood cell casts. The supernatant gave a strongly positive reaction for occult blood. A urinary urobilinogen test result was positive at 1:320. The total serum bilirubin level was 1 mg.%, 0.3 mg.% direct and 0.7 mg.% indirect. The erythrocyte sedimentation rate was 16 mm. per hour (Wintrobe).

Fluid intake was restricted, and the patient was placed on a low-salt diet. He complained of anorexia and generalized abdominal pain. On the fifth day of illness, the fluid intake was 1,170 cc., with a urinary output of 590 cc. The next day the urinary output fell to 60 cc. An electrocardiogram disclosed U waves and tall, peaked T waves in the precordial leads, suggestive of hyperpotassemia. The serum potassium level was 6.9 mEq. per liter, and the blood urea nitrogen level rose to 104 mg.%. Because of the marked oliguria and high concentration of serum potassium, the patient was transferred to the Medical College Hospital, Charleston, S. C., for consideration for artificial dialysis.

Therapy at the Medical College Hospital consisted of restriction of fluid intake and a low-protein diet. The highest blood urea nitrogen level was 152 mg.% on the 11th day of his illness. The antistreptolysin O (ASO) titer was 20 Todd units. Throat culture grew alpha-hemolytic streptococcus, Neisseria, and Staphylococcus albus. The result of a Coombs' test was negative, as was that of a red cell fragility test. Urine specimens obtained on the 13th and 14th days of his illness did not contain myoglobin, either on chemical or spectrophotometric examination.

Table 1.—*Urinary Findings in Nineteen Patients After Excessive Calisthenics**

Case, No.	Protein Mg.%†	Red Blood Cells	White Blood Cells	Casts	Globin
1	340	Present	...	...	...
2	100	Present	Present	Present	...
3	Present	...	Present	Present	OBP‡
4	100	...	...	Few	OBP
5	400	...	...	...	OBP
6	200	...	...	...	Myoglobin +
7	Present	...	Present	Present	Myoglobin +
8	400	Present	Present	Present	Myoglobin +
9	130	...	...	...	...
10	20	...	...	...	Myoglobin+
11	100	...	...	...	Myoglobin +
12	100	Present	Present	...	Myoglobin +
13	100	...	...	Present	...
14	75	...	...	...	Myoglobin +
15	1,500	Present	...	Present	OBP
16	500	Present	Present	Present	Myoglobin −
17	75	Present	...	...	Myoglobin +
18	80	...	...	Present	Myoglobin − Hemoglobin +
19	Present	...	...	Present	Myoglobin + Hemoglobin +

* Cases 1-18, squat jumps; case 19, squat thrust.

† Value in mg.% used in this column represents most abnormal of serial urinalyses.

‡ OBP signifies positive result of test for occult blood by orthotolidine (Hematest) method.

On the 10th day of illness the patient began to have diuresis, with urine outputs of up to 3,000 cc. daily. A 10-lb. weight loss occurred during diuresis, and the blood pressure returned to normal.

Kidney tissue obtained by needle biopsy (fig. 2) on the 10th day of illness revealed brown-pigmented debris in the tubular lumens and necrosis of the proximal convoluted cells in some regions. The only glomerulus present in the specimen appeared normal. The pathological diagnosis was hemoglobinuric nephrosis.

The blood urea nitrogen level gradually decreased to 19.4 mg.% by the 40th day. Two months after the onset of symptoms the phenolsulfonphthalein excretion was 40% in 15 minutes, with 70% excretion in one hour. The specific gravity of the urine after 14 hours of restricted fluid intake, 100 days after the onset of illness, was 1.033. An intravenous pyelogram showed no abnormalities. The patient resumed recruit training and subsequently was able to perform many squat jumps daily, without discomfort or abnormal urinary findings.

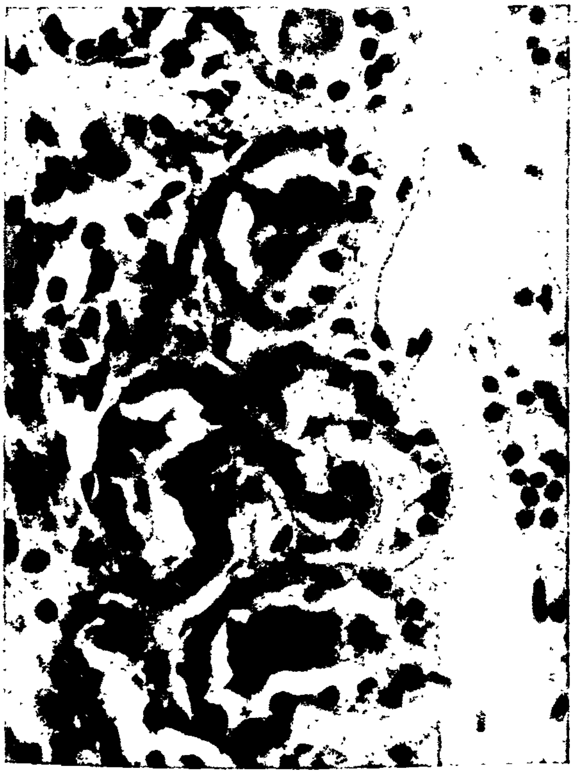

Fig. 2 (case 15).—Squat jump syndrome: photomicrograph of biopsy specimen of kidney, showing pigmented casts in three of four tubules on right (× 450).

Case 16.—This patient performed about 100 squat jumps. Three days later he passed dark urine and noted marked stiffness of both quadriceps muscles, which became firm and painful when flexed. He developed anorexia and had emesis on one occasion.

Physical examination disclosed moderate tenderness and marked firmness of the left quadriceps muscle, particularly over its lateral aspect. Urinalysis showed a protein level of 250 mg.%, with red blood cell casts and red blood cells in large quantities. The supernatant gave a strongly positive reaction for occult blood. The result of a myoglobin test on the same specimen was negative. After 14 hours of restricted fluid intake, the specific gravity was 1.023. Protein excretion in a 24-hour period was 1.35 Gm. The antistreptolysin O (ASO) titer was 250 Todd units. An intravenous pyelogram revealed no abnormalities.

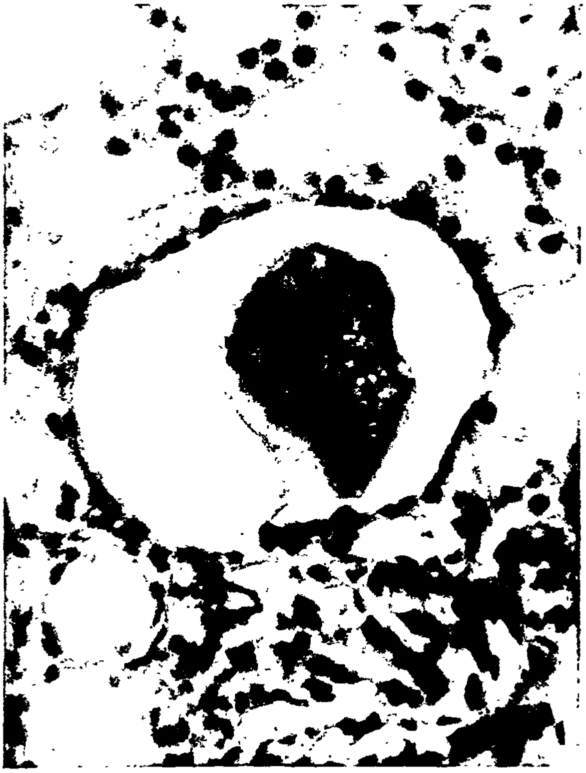

Fig. 3 (case 17).—Photomicrograph of biopsy specimen of left kidney, showing presence of large cast in dilated tubule whose epithelium is flattened (× 600).

A specimen of kidney tissue obtained by needle biopsy four months after the onset of the illness contained 10 glomeruli. Several glomeruli showed adhesions between Bowman's capsule and the glomerular tuft. A few glomeruli had extravasated red blood cells in the intercapsular space. No casts were noted, and the tubular epithelium appeared normal. The diagnosis was mild, subacute glomerulonephritis. Urinalyses performed during the five-month period of observation showed white blood cells, red blood cells, and albuminuria.

Case 17.—A 19-year-old recruit one day performed 95 squat jumps and the next day about 65 squat jumps. That evening his legs began to hurt. On the third day he passed coffee-colored urine.

About one year previously, a renal calculus had been removed from the right ureter. Since that time he had twice noted the passage of red urine after strenuous physical exertion.

On physical examination the patient could flex neither knee more than 30 degrees, and lateral moderate firmness and tenderness of the left quadriceps muscle were noted. The urine gave a strongly positive reaction for myoglobin and contained numerous red blood cells and 75 mg.% of protein. Values for serum uric acid, calcium, and phosphorus were normal.

Urinalysis continued to disclose microscopic hematuria for two weeks, the urine thereafter becoming normal. The patient was discharged to duty but was readmitted six weeks later for gross hematuria. Urinalysis on this occasion revealed 40 to 50 red blood cells per high-power field and a 30-mg.% level of protein. Sixty milligrams of protein were excreted in a 24-hour specimen. The 24-hour urine protein level rose to 722 mg. when collected during a day which included five hours of physical exertion. An intravenous pyelogram disclosed sharp renal calices, with some pelvic distortion on the right attributed to the previous operation. Urine cultures grew contaminants.

Table 2.—*Summary of Symptoms and Urinary Findings in Eighteen Patients with Squat Jump Syndrome*

	Findings in Patients, No.*	
	Present	Absent
Myoglobinuria	8	2
Albuminuria	18	0
Pyuria	2	16
Hematuria	6	12
Red blood cell casts	4	14
Oral temperature over 100F (37.8C)	4	13
Lumbar ache	6	7
Vomiting	6	6
Quadriceps swelling and tenderness	18	0

* In some instances total number of patients does not add up to 18 because test was performed in smaller numbers of patients or history was inadequate for documentation.

Renal tissue obtained by needle biopsy (fig. 3) 90 days after the squat jump syndrome appeared normal, with the exception of one dilated tubule whose lumen contained a brown granular cast. The epithelium of the dilated tubule was extremely thin, resembling an early stage of regeneration. The specimen contained 18 glomeruli. The diagnosis was resolving hemoglobinuric nephrosis.

Case 18.—A 19-year-old Marine performed 50 squat jumps and, within five hours began to observe pain and swelling in both quadriceps muscles. Four days later the patient began to pass dark brown urine which persisted for 48 hours. Emesis occurred on one occasion, and there was steady aching in both lumbar regions.

His temperature was 99.8 F (37.7 C), and the blood pressure 150/90 mm. Hg. There was moderate swelling and slight induration over both quadriceps muscles laterally.

A mahogany-colored urine specimen obtained at the time of admission showed a negative result of a myoglobin test but a positive one for hemoglobin. On spectrophotometric study, a sample of this urine was found to have a wave length identical to a methomoglobin solution placed in a control specimen of urine.[3] There were 80 mg.% of protein and many brown granular casts in the initial urine specimen. The urinary urobilinogen dilution was 1:80. The total serum bilirubin level was 0.8 mg.%, 0.4 mg.% indirect. The blood urea nitrogen level was 17.5 mg.%. The total urinary 24-hour excretion of protein the day of admission was 1.47 Gm.

Serum glutamic oxalacetic acid transaminase (SGO-T) levels, determined at 12-hour intervals during the first three days of hospitalization, ranged from 70 to 76 sigma frankel units (normal is 40); they fell to 21 units three weeks later.

Case 19.—An 18-year-old recruit performed many squat thrusts. (This calisthenic primarily involves the muscles of the arms and shoulders.) That evening he became nauseated, passed rust-colored urine, and began to have pain in the lateral portion of the deltoid muscles. Physical examination disclosed only minimal tenderness over the painful areas of muscle.

The urine specimen taken on admission was dark brown in color and gave a positive reaction for protein, with many granular casts. There was a trace of myoglobin and a moderately positive reaction for hemoglobin (Blondheim's method [2]). Spectrophotometric analysis of this specimen disclosed a small quantity of metmyoglobin, most of the urinary pigment being due to methemoglobin.[3]

The patient's urine returned to a normal color during his first day of hospitalization, but he continued to complain of muscle pain for several days. Subsequent attempts to reproduce hemoglobinuria, by a prolonged march and extensive calisthenics of the upper extremities, were unsuccessful.

Comment

The urinary abnormalities seen in the 18 cases of squat jump syndrome are tabulated in table 2. The myoglobin test gave positive results in 8 of the 10 patients on whom it was performed. It seems probable that the two negative results were due to failure to obtain a urine specimen early enough in the course of the illness, at a time when myoglobinuria was still present. Intravenous pyelograms were obtained for five patients. The only abnormality was the pelvic disortion mentioned above in case 17.

Duration and Possible Etiology of the Urinary Pigments.—The urine test for myoglobin gave positive results for only a brief period, probably less than 48 hours. All positive results of tests for myoglobin were obtained at the dispensary prior to hospitalization. No hospitalized patients exhibited myoglobinuria, although they frequently passed dark urine during their first day of admission. The significance of this observation became apparent when the patient in case 18, the final case of squat jump syndrome, appeared. This patient's dark urine was spectrophotometrically proved to contain methemoglobin. It seems possible that the dark urine passed by the other hospitalized patients, which was myoglobin negative, would have contained hemoglobin had it been examined for such. Some support for this impression can be gained by the observation that dark urine specimens taken from six patients with squat jump syndrome, and examined spectrophotometrically prior to this study,[3] were all found to contain methemoglobin without evidence of myoglobin. The urine specimen obtained from the patient in case 19, whose exertion and physical findings were in the upper extremity, contained both metmyoglobin and methemoglobin.

To summarize, myoglobinuria was seen only during the initial phase of squat jump syndrome. It is believed that the pigment causing the dark color of urine later in this syndrome is hemoglobin.

Case 19 appears noteworthy for two reasons. This case proved that both myoglobin and hemoglobin could be contributing to the dark urine passed by a person who has performed excessive calisthenics. It also demonstrated that exercise producing minimal physical findings could, nevertheless, be responsible for myoglobinuria and hemoglobinuria. It is important that this patient's urine contained no red blood cells which could have caused hemoglobinuria if partially hemolyzed.

Ono,[4] by a sensitive serologic technique, has demonstrated that myoglobinuria is seen in skaters, runners, and persons undergoing electric shock therapy. In the latter subjects myoglobinuria was maximal after the second electric shock treatment and had disappeared completely by the sixth course of electric shock therapy. The disappearance of myoglobinuria after repeated convulsions suggests that skeletal muscle may be altered by such violent exertion. No recruit who had experienced squat jump syndrome ever had a recurrence of muscle symptoms after resuming execution of the squat jumps. The ability to resume performance of squat jumps without difficulty suggests that muscular changes similar to those observed by Ono may have occurred during violent squat jumping.

A quadriceps biopsy specimen (fig. 4) obtained from the patient in case 14 three days after the onset of swelling revealed edema of the skeletal muscle and adjacent connective tissue. Red blood cells were seen scattered diffusely through the connective tissue, with clumps in one region of the muscle. The presence of red blood cells in this biopsy specimen could be an artefact of surgery. However, in view of the marked muscle swelling seen in the squat jump syndrome, it seems reasonable that some red blood cells, as well as plasma, might escape from the muscle capillaries. Hemolysis of these cells could be the source of the hemoglobinuria. Another possibility is intravascular hemolysis of red blood cells, secondary to release of a toxic material from damaged muscle tissue.

Whether hemolysis of extravasated red blood cells could constitute the explanation for march hemoglobinuria is unclear. The only recruit seen with march hemoglobinuria during this period did not have muscle symptoms.

Nature of the Renal Lesion.—Intravenous hemoglobin has been shown by Miller and associates[5] to have renal vasoconstricting properties. Whether myoglobin similarly causes renal vasoconstriction is uncertain. Any process which damages muscles severely enough to cause myoglobinuria may well release other substances into the blood (transaminase, adenosine triphosphate [ATP], aldolase, lactic acid, and others). At least one of these (ATP) has been shown to have a physiological effect which would be deleterious to the kidney (hypotension).[6]

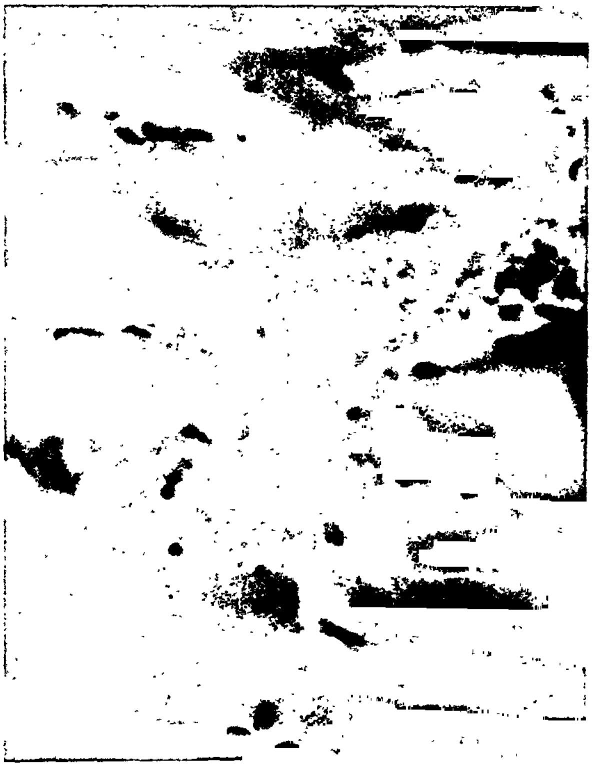

Fig. 4 (case 14).—Photomicrograph of biopsy specimen of quadriceps muscle: note presence of scattered red blood cells between muscle fibers (× 400).

The urinary findings were most marked during the period when dark urine was being passed. It seems possible that these abnormalities were due to transient renal vasoconstriction, caused by hemoglobin and perhaps other muscle products. Possibly, a reduced blood volume secondary to plasma loss within the quadriceps muscle may have contributed to the renal damage.

The renal biopsy specimens obtained in cases 15 and 17 showed clear evidence of tubular pathology typical of acute renal failure.[7] The clinical course of the patient in case 15 was typical of acute renal failure, while the patient in case 17 had no azotemia or evident oliguria. The patient in case 15 exhibited high fever and mental confusion; it is possible, therefore, that heat stroke as well as squat jump syndrome may have contributed to the acute renal failure.

The patients in cases 1 and 16 had persistent albuminuria, with intermittent microscopic hematuria, after incurring the squat jump syndrome. The renal biopsy tissue in case 16 presented an appearance compatible with subacute glomerulonephritis. It seems possible that the patients in cases 1 and 16 may have had glomerulonephritis prior to, or simultaneous with, the squat jump syndrome and that their renal disease became manifest when they required medical attention. However, there is no way of completely excluding the possibility that their persistent urinary abnormalities are due to the deleterious renal effects of squat jumping.

Review of Literature for Similar Cases.—De Langen[8] reported myoglobinuria in a prisoner of war forced to do excessive genuflections. The swelling of the quadriceps muscle and the transient oliguria with azotemia experienced by this patient were similar to the clinical course of the squat jump syndrome in the patient in case 15.

Pearson and associates[9] discovered myoglobinuria in a patient who had undergone prolonged skipping on a hard pavement. Initially, there was swelling of the muscles of the anterior tibial compartment followed by muscle atrophy in the recovery period. This patient exhibited albuminuria for five days.

Stahl[10] reported five cases of passage of dark urine after excessive calisthenics. Two of his patients had painful muscles in the arms, while three had painful muscles in the legs. Urinary findings in these patients included albuminuria, hematuria, and red blood cell casts.

Differential Diagnosis.—The hematuria, albuminuria, and red blood cell casts seen in exertional myoglobinuria and hemoglobinuria are identical with the classic urinary findings in acute glomerulonephritis. In a person who has a history of strenuous physical exertion prior to the discovery of urinary abnormalities, it is of vital importance not to attribute the dark color of the urine to the presence of red blood cells or to dehydration without further investigation. If such a dark urine specimen can be proved to contain myoglobin, a diagnosis of acute glomerulonephritis is unlikely to be correct. Similarly, the finding of hemoglobin in a urine specimen which doesn't contain red blood cells has some diagnostic value if the urine sample is fresh.

Other features of value in excluding acute glomerulonephritis from exertional myoglobinuria are (1) a history of excessive repetitive physical exertion, particularly significant if it is a type of exertion to which that person is unaccustomed; (2) subjective complaints of muscle soreness, or evidence of swelling and tenderness in the exerted muscles, or both; (3) normal serum antistreptolysin O (ASO) titers, negative throat cultures, without history of pharyngitis; (4) transient proteinuria and hematuria, accompanied by passage of dark urine with a total duration of less than one week; and (5) a renal biopsy specimen disclosing tubular necrosis with casts, in contrast to the changes of acute glomerulonephritis.

Alyea and Parish[11] demonstrated that hematuria and albuminuria are consistently present in well-conditioned persons after strenuous physical exertion. The albuminuria and hematuria have been attributed to renal ischemia, secondary to increased blood flow to skeletal muscle. These persons do not give a history of dark urine and muscle swelling and tenderness are absent. The observed urinary abnormalities are proportional to the severity of the exertion and are regularly reproduced by repetition of the exertion. Hence, this condition is unlike the squat jump syndrome, which does not appear to be reproducible.

Summary

The squat jump syndrome, 18 cases of which are reported, is characterized by painful swelling of the quadriceps muscles after their extensive repetitive exertion, and by dark urine containing myoglobin and hemoglobin. The albuminuria, hematuria, and casts in the urine of these patients may have been due to the adverse renal effects of prolonged vasoconstriction associated with hemoglobinemia. It is possible that decreased plasma volume, secondary to loss of plasma within the quadriceps muscle, was contributory. Renal biopsy specimens taken from two of these patients demonstrated brown granular casts and tubular abnormalities similar to the pathological findings in acute tubular necrosis.

Valuable features in distinguishing the albuminuria, hematuria, and casts that follow prolonged, unaccustomed exertion from acute glomerulonephritis are: passage of dark urine after excessive exertion, sore swollen muscles, myoglobinuria, normal serum antistreptolysin O (ASO) titers, and renal biopsy specimens. Renal biopsy specimens distinguished the tubular pathology seen in squat jump syndrome from the glomerular lesion of acute glomerulonephritis in three diagnostic problem cases.

In one additional case, myoglobinuria and hemoglobinuria followed prolonged exertion of the upper extremity. The hemoglobinuria which follows prolonged exertion may be due to the hemolysis of extravasated red blood cells within the swollen muscles.

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The Commanding Officer of the Marine Recruit Department at Parris Island, S. C. assisted this study by granting permission to interview drill instructors and physical therapy personnel. Drs. David P. Earle and Cheves Smythe acted as consultants in the preparation of this article. Dr. R. H. Gadsden performed the spectrophotometric studies.

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BENEFICIAL EFFECTS OF HYPOTHERMIA AFTER CARDIAC ARREST

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Cardiac arrest occurred in a 2-year-old girl. Hypothermia was produced with a water-cooled mattress. Despite the presence of hypertonicity, convulsions, and coma in the immediate postarrest period, the patient made a complete neuropsychological recovery. The high mortality and residual nervous system damage that follow cardiac arrest are usually due to cerebral hypoxia. The duration of hypoxia generally determines the prognosis. Individual variations modify the ability to withstand hypoxia without resulting permanent brain injury. Preexisting vascular disease, age, and the presence of hypoxia before arrest are factors that determine the degree of injury. The cessation of cerebral blood flow for more than three to four minutes is usually followed by cortical cellular destruction.

The successful reduction or prevention of neurological sequelae after cardiac arrest of five or more minutes by use of hypothermia has been reported by Williams and Spencer.[1] Their observations have been confirmed by a study of dogs.[1] The effectiveness of this method of therapy has not been widely reported or substantiated by other observers. The case report presented here describes the use of hypothermia in an attempt to prevent further central nervous system damage after acute hypoxia occurring after cardiac arrest.

Report of a Case

A 2-year-old girl was admitted to the Long Island Jewish Hospital on Feb. 14, 1959, with a diagnosis of epiglottitis with croup. Because of obstruction in the upper part of the airway and respiratory distress, a tracheotomy was performed one hour after admission.

The child responded satisfactorily until 6 a. m. on the morning of the third postoperative day, when she developed cyanosis and difficulty in breathing. Examination at this time showed a pulse rate of 120 per minute, a respiratory rate of 28 per minute, and diminished breath sounds in both lungs. Oxygen was administered directly into the tracheotomy tube, and slight improvement was noted. The patient continued to be restless, dysp-

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neic, and intermittently cyanotic. At 11:30 a. m. 0.3 mg. of digoxin was given intramuscularly and 75 mg. of hydrocortone was given by intravenous infusion. At 12 noon the patient was brought to the operating room for an emergency bronchoscopy. A large crust of mucus was observed at the carina but could not be removed through the bronchoscope. Suctioning through the tracheotomy stoma with a large rubber catheter yielded some thick mucus. At this point the patient became apneic, and a peripheral pulse could not be felt. The pupils were widely dilated. An endotracheal tube was immediately inserted into the tracheotomy stoma, and artificial respiration with oxygen was begun. The chest was opened within one minute, the diagnosis of cardiac arrest confirmed, and cardiac massage begun. The heart began beating spontaneously after two minutes of massage. The chest was closed and thoracotomy tube drainage instituted. The child was taken to the recovery room in a semicomatose state with generalized muscular hypertonicity. The respiration and pulse rates were good. Hypothermia was immediately induced with a water-cooled mattress. The body temperature fell from 38 to 36 C (100.4 to 96.8 F) within two hours, reached 33 C in another four hours, and was maintained at 31.5 to 33.0 C (88.7 to 91.4 F) during the 48-hour period of hypothermia.

Twenty-four hours after cardiac arrest there was an increase in the generalized hypertonicity, followed shortly by a grand mal convulsive seizure. The seizure was controlled with 25 mg. of diphenylhydantoin (Dilantin) sodium administered intravenously. Forty-eight hours after cardiac arrest the patient began to respond to questioning by opening her eyes and turning her head. At this point hypothermia was discontinued and, after twelve hours, the body temperature rose slowly to 36.5 C (97.7 F). Five days after cardiac arrest the patient regained full consciousness, recognized her parents, and was able to take fluids by mouth. Two weeks after cardiac arrest, neurological evaluation gave completely normal results except for slight hesitation in walking.

The child was discharged from the hospital on the 21st day after cardiac arrest. Six months later she was submitted to a battery of psychological tests by a psychiatrist and psychologist. These tests indicated the patient to be a bright, well-adjusted child with scores which were normal or above normal.

Comment

This patient recovered from the effects of both acute and chronic lack of oxygen. As early as six hours prior to cardiac arrest the patient undoubtedly suffered from cerebral hypoxia as evidenced by semistupor, restlessness, tachypnea, and cyanosis. One can only speculate as to the actual cause of cardiac arrest, but the probable course of events was that of a hypoxic myocardium finally succumbing to the episode of acute oxygen deprivation occasioned by the attempts at bronchoscopy and tracheal suctioning.

Tracheotomy was beneficial as it permitted the patient to have rapid and effective artificial ventilation with oxygen as soon as the arrest occurred. Furthermore it reduced the total respiratory dead space and permitted easy access to accumulated tracheal secretions.

Hypothermia in the immediate post-arrest period prevented the rapid rise in body temperature, which is a frequent accompaniment of cerebral hypoxia. Despite such poor prognostic signs as hypertonicity, convulsions, and persistence of a semistuporous state for about 48 hours, this patient went on to full neurological recovery. It would appear that the prompt institution of hypothermia was largely responsible for this complete recovery from severe cerebral hypoxia.

The high mortality and residual nervous system damage that follows cardiac arrest is usually due to cerebral hypoxia.[2] The duration of hypoxia generally determines the prognosis.[3] Individual variations modify the ability to withstand hypoxia, without resulting permanent brain injury. Preexisting vascular disease, age, and the presence of hypoxia before arrest are factors that determine the degree of injury. The cessation of cerebral blood flow for more than three to four minutes is usually followed by cortical cellular destruction. Cooley [11] has pointed out that in youngsters already hypoxic, one minute of cardiac arrest has resulted in cerebral damage. Hypoxia affects the brain by direct injury to the nerve cells and cerebral swelling. The reversibility and extent of nerve cell injury is not well understood.[4] The cerebral swelling results from the increased permeability of the capillaries due to hypoxia, with a resultant loss of fluid from the capillaries into the intracellular and intercellular spaces.[5] The increase in brain volume exceeds the capacity of the subarachnoid space, with a resultant blockage of spinal fluid circulation, herniation of the brain stem, local tissue necroses, neuron damage, and petechial hemorrhages.[6]

In the past, the major emphasis in the treatment of cardiac arrest has been directed toward restoring the heartbeat and reestablishing circulation. Little attention has been paid to the problem of preventing further brain damage by decreasing cerebral metabolism and cerebral swelling. To accomplish this, Williams and Spencer [1] used hypothermia in four patients and stopped the cerebral circulation for five minutes. Three of the patients recovered completely, and the fourth survived with moderate neurological injury. The effect of hypothermia on the nervous system has been widely studied. Significant reduction of brain swelling has been noted[7] during craniotomy in patients who have been rendered hypothermic. At 30 C (86 F) it has been estimated that a 4% reduction in brain volume occurs; this is equal to a 30% increase in intracranial space of an adult.[8] Hypothermia also controls and reduces the febrile response (39 to 40 C, or 102 to 104 F) that often accompanies cerebral injury. The hyperpyrexia, with its accompanying increase in metabolism and oxygen demand, places an additional burden on an already damaged nervous system.[9]

Rosomoff and Holaday[8] estimated that at 28 to 30 C (82 to 86 F) the oxygen needs of the brain are reduced 50%. Hypothermia, by decreasing the oxygen demands, protects the brain against hypoxic injury. This is an important factor in patients with an embarrassed cerebral circulation as a result of increased intracranial pressure.

Other techniques for reducing cerebral edema after anoxia have been tried clinically. Human albumin given intravenously and 30% urea in 10% dextrose solution have been used.[10] The clinical experience with these substances is still too small to permit valid conclusions to be drawn.

Airway management in comatose patients is equally important in controlling cerebral swelling. Respiratory obstruction can produce further increase in cerebral edema and vascular engorgement. White and others[5] demonstrated that anoxia produces edema of the nervous system and that the increase in blood PCO_2 level results in cerebral vascular engorgement.

This single case report, like the others reported in the literature, permits no valid conclusion to be drawn until control studies can be undertaken.[1] Experience has demonstrated that patients who are hypoxic before cardiac arrest frequently develop neurological sequelae.[11] Patients who show evidence of cerebral damage such as convulsions, hyperpyrexia, hypertonia, and coma for more than 24 hours respond poorly.[2c] This patient, despite all indications for a poor prognosis, recovered without any evidence of central nervous system damage.

It is our belief that, after cardiac arrest, the patient's temperature should be reduced to 31.5 to 33 C (89 to 91 F) and maintained there until neurological functions return to an optimal state. In conjunction with hypothermia, maintenance of a patent airway is mandatory. This can best be accomplished initially by the insertion of an endotracheal tube. Then, after adequate oxygenation has been attained, a tracheotomy can be performed to facilitate tracheal suctioning by the nursing staff and to reduce considerably the respiratory dead space. The management of such patients requires constant supervision and teamwork. In this case it was only through the concerted action of the surgeon, anesthesiologist, pediatrician, and nursing staff that a gratifying result was obtained.

Summary

Cardiac arrest occurred in a 2-year-old girl. Hypothermia with a water-cooled mattress was begun immediately after the arrest. Despite the presence of hypertonicity, convulsions, and coma in the immediate postarrest period, the patient appeared to have made a complete neuropsychological recovery. It is only by use of this technique in numerous other similar cases that a valid conclusion can be obtained as to the beneficial effects of hypothermia after cardiac arrest.

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Irving L. Bauer, M.D., and Milton Kauffman, Ph.D., performed the psychological tests on the patient in this study.

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CLINICAL NOTES

TOXICITY OF VITAMIN K

INDUCED HYPOPROTHROMBINEMIA AND ALTERED LIVER FUNCTION

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and
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Among the more patent abuses in present-day therapy is the indiscriminate administration of vitamin K and its analogues. Free use of these substances is made on the assumption that they are harmless, and the physician generally believes that he is doing something of real value for his patient by giving him vitamin K during a hemorrhagic episode, be it bleeding from a tonsillar fossa, a prostatic bed, or a duodenal ulcer. Rarely is such hemorrhage due to a defective coagulation mechanism, and the drug is generally given without prior evaluation of the prothrombin activity of the patients' blood.

In the face of predetermined hypoprothrombinemia, it is likewise common practice to give vitamin K in greater than adequate doses and to continue the treatment well beyond the time required to correct a true deficiency. Hypoprothrombinemia due to a seriously diseased liver cannot be corrected by vitamin K therapy, and many patients with this disorder may actually be harmed by frantic administration of menadiol (Synkayvite) sodium diphosphate or phytonadione (Mephyton), the only benefit being realized by the manufacturer.

One should not be very censurious of physicians using vitamin K, however. The medical literature is virtually devoid of data relating to toxic effects of vitamin K. Only one[1] of five standard textbooks of pharmacology that we consulted made mention of the possibility of such effects, limited to the comment that hypoprothrombinemia could be induced by giving excessive amounts. Thus, we believe that a recent experience in our hospital is worth recounting in this respect, along with a summary of pertinent experimental and clinical reports, however few.

Report of a Case

An 80-year-old woman was admitted on Feb. 13, 1959, with the established diagnosis of carcinoma of the rectum. Studies preparatory to an abdominoperineal resection gave quite normal results except for a prothrombin time of 18 seconds (40%). Her liver was not enlarged, her previous nutritional status had been good, and no history of alcoholism was obtained. Two days later the prothrombin time was again determined and was found to be 15.5 seconds (69%).

On Feb. 16 she was given 150 mg. of menadiol sodium diphosphate intramuscularly and 50 mg. of phytonadione intravenously. The operation was performed the next day without undue bleeding. Inspection of liver disclosed no gross abnormalities. Vitamin K therapy was continued thereafter, the patient receiving 30 mg. of menadiol sodium diphosphate intramuscularly each day for 11 days, supplemented by 50 mg. of phytonadione by vein on days 8 through 11, despite the fact that her prothrombin time had reached the normal of 13 seconds (100%) by the fourth postoperative day. Subsequently there was a fall in prothrombin activity to 29% of normal by the 12th postoperative day (see figure), and an increasing hemorrhagic ooze from the perineum became troublesome.

Consultation with the hematology service resulted in transfusions of fresh blood and discontinuance of treatment with vitamin K analogues. We also found that certain liver function tests were out of order (see figure and table). Her prothrombin time returned to normal in three weeks. Her sulfobromophthalein retention rose to 35.4% on the 34th postoperative day and returned to normal nine days later. After three months liver function appeared to be quite normal.

Comment

Massive doses of vitamin K administered to experimental animals have been reported to cause anemia (mechanism unspecified);[2] produce aplastic anemia, petechial hemorrhage, and renal tubular degeneration;[3] bring about vomiting, albuminuria and porphyrinuria;[4] and provoke focal hemorrhages in many organs.[5]

Premature infants given large doses of the water-soluble analogue of vitamin K have developed hemolytic anemia and kernicterus.[6] Beamish and Storrie[7] also reported a severe hemolytic reaction after the intravenous injection of 50 mg. of phytonadione.

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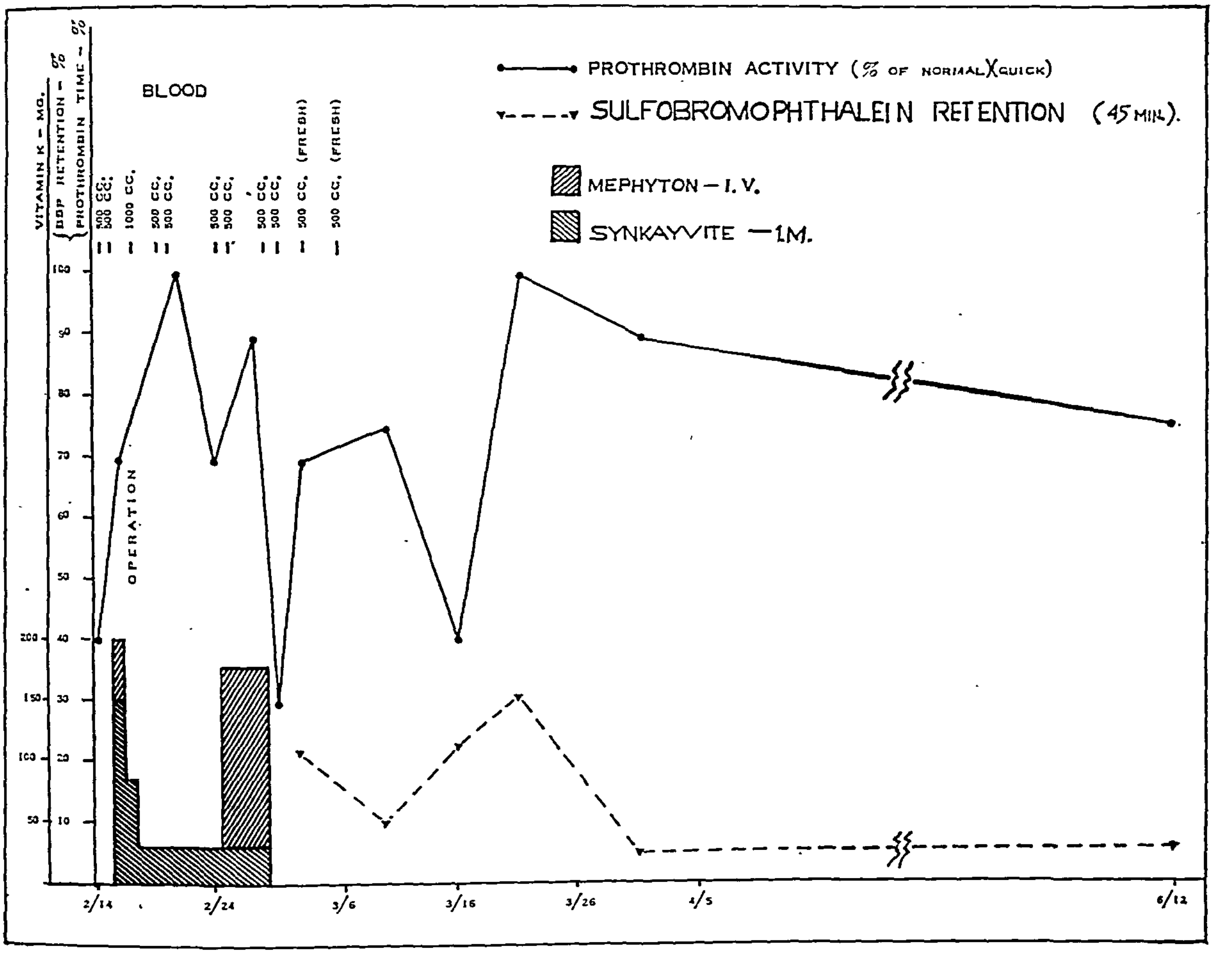
A few articles mention the occurrence of depression of prothrombin activity after administration of vitamin K in high dosage to patients with diseased livers.[8] Steigmann and others,[8b] in connection with their report, recommended reevaluation of the indications for vitamin K therapy as well as modification of dosage. Kaplan[8c] also noted reduced prothrombin activity in patients with severe liver disease who were given large doses of menadiol sodium diphosphate (75 mg.) and whose activity returned to normal when 10-mg. doses were substituted. The same observation was made by Unger and Shapiro[8d] during their evaluation of vitamin K tolerance as a measure of hepatic function.



Graph showing prothrombin activity and sulfobromophthalein retention in 80-year-old woman.

Our patient is apparently the second one reported with normal liver function in whom hypoprothrombinemia was induced by administration of vitamin K, the other being included in the series of Unger and Shapiro.[8d] Ours seems to be the first record of significant alteration of other liver function tests after K-hypervitaminosis, with resumption of normal function after withdrawal. We are reasonably sure that this same sort of thing must have happened countless times and gone undetected because liver function tests had not been performed at the proper times. We regret that we did not obtain complete coagulograms throughout our patient's course, including determination of labile and stable factors. Perhaps others will fill this gap.

Thus our experience, coupled with the few reports in the literature, indicates that vitamin K is by no means innocuous. We agree with Steigmann and others[8b] that vitamin K therapy should be discontinued if no improvement in prothrombin activity occurs within 48 hours after administration of the drug. We recommend further that patients with hypoprothrombinemia who respond favorably to vitamin K therapy be given no more than is necessary to restore prothrombin activity to normal.

Conclusions

Vitamin K and its analogues possess toxic properties that can induce hypoprothrombinemia and other alterations in liver function if drugs containing this vitamin are administered in excessive dosage or over prolonged periods. These drugs should not be prescribed unless hypoprothrombinemia, not assumption is made that the deaths occurring within 10 days of thermal injury are more likely to be related to the effects of shock or its treatment than are subsequent fatalities. The deaths from burns that occurred within 10 days of the injury were, in every instance, among persons who were given whole blood in the first 48 hours. That a balanced salt solution is adequate treatment for shock due to burns is attested to by the absence of mortality for 10 days after the burn in the group which received saline but no blood.

Table 1.—*Parkland 1952-1956 Series Showing Mortality According to Burn Area and Treatment**

	Mortality, %					
	First 10 Days		Total		Patients, No.	
Burn Area, % Body Surface	Blood-Saline	Saline Only	Blood-Saline	Saline Only	Blood-Saline	Saline Only
15-24	0	0	0	1.5	4	65
25-44	8	0	25	2.5	12	39
45-64	67	0	89	30.0	9	13
Total					25	117

* Tracheobronchial burns excluded; patients less than 61 years of age.

When all deaths are included and only the more severe burns are reviewed, as seen in table 2, the differences in total mortality are significant in the group with 30 to 44% of the body surface burned—27% mortality for those receiving blood as a part of therapy for shock and 4% mortality for those receiving only a balanced salt solution. The mortality difference for the group with more extensive burns (45 to 64% of the body surface burned) is highly significant. The 89% mortality for the blood-saline group compared to 36% mortality for the saline solution only group indicates that a balanced salt solution can be used effectively and safely in extensive burns as well as those involving limited areas of the body.

The same mortality differences for the two kinds of therapy for shock are found in table 3, when mortality is correlated with the depth of burn in addition to the extent of the burn. The burn index refers to all the third degree burns but takes into account only one-half of the area involved with second degree burns; thus, the index is weighted to reveal the effect of deep burns.

Table 2.—*Parkland 1952-1956 Series Showing Mortality Between Groups According to Burn Area**

	Blood-Saline		Saline Only		Total Mortality, %		
Burn Area, % Body Surface	Burned, No.	Died, No.	Burned, No.	Died, No.	Blood-Saline	Saline Only	p
30-44	11	3	28	1	27	4	0.03
45-64	9	8	14	5	89	36	0.006

* All deaths included; patients less than 61 years of age.

The correlation between high total death rates and early treatment with blood-saline may appear to reflect that, by chance, patients with lethal burns were selected to be treated with blood-saline. We do not think this is true; any difference in inherent severity of burns based on differences of area or depth that exist between the two therapeutic groups could not have influenced the results, because comparisons of mortality have been made between burns of similar size and depth. Some factors that may have influenced mortality other than the treatment variable have been reviewed; for example, the mean age of the patients is 26 years for the blood-saline group and 22 years for the saline solution only group. The frequency distribution of ages in the two groups is not widely discrepant; 33% of the patients treated with blood-saline and 41% of the saline only series were under 15 years of age; 9% of the blood-saline group and 6% of the saline solution only group were over 50 years old. The two series were not characterized by differences relative to the seasons of the year in which the burns occurred, to the time interval between injury and the beginning of treatment, or to the method by which the thermal injury was incurred (conflagration or scald). If some abstruse means of selection had been operative, the mortality expectancy of the Parkland blood-saline series should be inherently greater for burns of given extent than that found in other reported series.

Table 3.—*Parkland 1952-1956 Series Showing Mortality According to Depth and Extent of Burn**

	Mortality, %					
	First 10 Days		Total		Patients, No.	
Burn Index†	Blood-Saline	Saline Only	Blood-Saline	Saline Only	Blood-Saline	Saline Only
4-24	0	0	0	2	6	95
25-44	9	0	27	6	11	17
45-64	75	0	100	60	8	5
Total					25	117

* Tracheobronchial burns excluded; patients less than 61 years of age.
† All third degree + ½ second degree burn area.

The mortality expectancy can be derived by means of probit analysis which establishes a straight-line relationship between the size of the burn and the mortality. At various points along this line, one can determine the size of burn that is expected to be 10% fatal, 20% fatal, or 30, 40, 50, up to 100% fatal. The area of burn that is lethal in 50% of patients is arbitrarily used in comparisons of results to represent the entire series and is referred to as LA_{50}. This device obviates the complicated comparison of slopes of lines when evaluating the effectiveness of treatments used in different series.

In table 4, the LA_{50} of the 1952 to 1956 Parkland blood-saline treated series of burned patients does not differ significantly ($p = 0.3$) from another series of burned patients treated with blood and saline that was previously reported[2] from Dallas, Texas, and Kankakee, Ill. The LA_{50} of the blood-saline series is nearly identical with that obtained in a combined series from Dallas, St. Louis, and Kankakee, in which several kinds of early treatment (plasma-saline, plasma-water, blood-saline) were used. The similarity of mortality expectancies is strong refutation of the hypothesis that the Parkland blood-saline series of patients was selected, and most likely this series did not include more fatally burned persons than would be expected to occur except by random. The relatively poor survival rate of the patients treated with blood and saline in Parkland Hospital as compared to the survival rate of those treated with a saline solution only is thought to be a function of the safety and efficacy of saline, only. In corroboration, table 5 shows the mortality expectancies for the Parkland patients who were treated early with saline solution only and for combined series of patients to whom blood and saline solution were given. A higher rate of death expectancy was found in patients with all sizes of burns when blood-saline was used during the shock phase.

Causes of Death: The deaths occurring in the first 10 days in the 1952 to 1956 Parkland series were all in the group which received blood in the first 48 hours, and these deaths were predominantly due to respiratory insufficiency. Postmortem examinations revealed a high incidence of pulmonary congestion, atelectasis, edema, and pneumonitis, as listed in table 6. The lungs were often heavy and noncrepitant. Since tracheobronchial burns are excluded, these findings are probably related to the effects of the peripheral burns or to the treatment.

TABLE 4.—*Comparison of Lethal Area (LA$_{50}$) Among Three Series of Patients with Thermal Injury**

Therapy	LA$_{50}$†	
Blood-Saline, Parkland 1952-1956	48	p=0.3
All Therapy,‡ Combined Series 1944-1952	49	
Blood-Saline,‡ Dallas, Texas; Kankakee, Ill. 1944-1952	55	

* Patients less than 61 years of age.
† Derived from probits.
‡ Data reported by Moyer.[2]

As a result of these clinical observations, experiments were performed in our surgical laboratories to see whether burns which did not involve the tracheobronchial tree had any effect on respiratory function. It was found that deterioration in respiratory dynamics begins immediately after burning. In experimental scalds of 31 dogs produced by 30-second immersion of 40% of body surface in water heated to 85 C, Steph and colleagues[3] found a fall in total lung volume and a pronounced decrease in pulmonary compliance. The effects of different modalities of volume-replacement therapy were differentiated by giving one group of burned dogs lactated Ringer's injection (10% of body weight) and another group whole blood (3% of body weight). When lactated Ringer's injection (Hartmann's solution) was infused intravenously as treatment for the shock due to burn, the pulmonary compliance was found to improve, and, five hours after the burn, 60% of the animals had regained values of elastic compliance of the lung which exceeded those of the preburn state. When whole blood was given intravenously to combat shock due to burn, the compliance of the lungs continued to fall, and, five hours after the burn, 70% of the dogs were found to have a decreased compliance.

TABLE 5.—*Mortality Expectancy Derived from Probits**

Burn Area, % Body Surface	U.S. 1946-1951† Probit $Y = 1.63 + 0.0592x$‡	Parkland 1952-1956§ Probit $Y = 1.71 + 0.050x$
20	0.014	0.011
30	0.055	0.04
40	0.16	0.10
50	0.34	0.21
60	0.57	0.39

* Analysis includes all patients less than 61 years of age.
† Values for expected mortality (1.0 = 100%; 0.75 = 75%) in blood-saline series were computed by Moyer[2] and serve as reference for gross assessment of results achieved in Parkland Hospital by treatment of burns with buffered saline only during first two days after injury.
‡ % Body surface.
§ Saline only series.

Baxter and DeCosse[4] have demonstrated by pulmonary function and blood-gas studies (decreased arterial oxygen saturation with variable carbon dioxide pressure) in burned men that respiratory insufficiency begins early after burning and persists, often causing death several days later. All of their patients received colloid or whole blood treatment during the shock phase.

Use of Colloid Solutions: Some clinicians believe that colloid solutions, other than whole blood, are essential in treating burn shock. Rather than attack this thesis on theoretical considerations, a more valid refutation is presented in table 7, which compares the mortality expectancies of burned persons in whom shock is treated, with or without colloid. The mortality expectancies have been derived from probits, as recommended by Moyer,[2] so that the relative efficacy of different modalities of treatment used in one hospital may be assessed. All forms of treatment for shock were effective in patients with burns of 20 and 30% of the body, but patients with more extensive burns revealed wide discrepancies in mortality expectancy, depending on the form of therapy. For example, patients with burns that cover 60% of the body have 94% mortality expectancy when treated with normal human plasma but only

TABLE 6.—*Parkland 1952-1956 Series Showing Causes of Death**

Cause	Early Deaths†		Late Deaths‡	
	Blood-Saline	Saline Only	Blood-Saline	Saline Only
Pulmonary				
Bronchopneumonia	4	0	1	...
Congestive atelectasis	2	0	...	...
Pulmonary edema	6	0	...	...
Aspiration asphyxia	...	...	...	3
Renal				
Tubular necrosis	1	0	...	...
Septicemia	2	0	4	3
Enterocolitis	0	0	1	...

* Tracheobronchial burns excluded.
† Occurred within 10 days of burn.
‡ Occurred after 10 postburn days.

39% mortality expectancy when treated with saline solution only. The lowest mortality expectancy of the three groups occurred in the saline series for burns of every size, whereas the worst results were expected in the plasma series. The mortality of the Parkland saline series is compared in table 8 with the mortality that attended the use of colloid solutions in a combined series from St. Louis City Hospital; Homer G. Phillips Hospital, Dallas, Texas; and Kankakee Clinic, Kankakee, Ill. It is apparent that the omission of plasma or other colloid from the treatment of shock due to burns does not adversely affect survival rate.

Although not routinely needed, normal human plasma may be used, with variable benefit in the management of two exceptional types of burned persons. One is the cachectic or malnourished person whose protein stores were depleted before the burn was incurred. This chronic starvation state may be associated with a poor hemodynamic and functional response to the infusion of quantities of salt solution which ordinarily effect recovery in other persons. Although this poor response to salt solutions usually portends a fatal outcome for the patient, the infusion of plasma has occasionally caused temporary improvement.

The other instance in which plasma may be used in burn shock is in management of the burned infant. Markley and colleagues[5] have reported that survival was improved in infants when plasma was used in a controlled clinical study conducted at Lima, Peru. Alternate, burned patients were given crystalloid solutions only, and no advantage to the use of plasma could be shown, except in infants.

Only plasma which has been stored for six months at room temperature should be used, for the limited benefits of plasma infusion do not warrant the great risk of homologous serum hepatitis that attends the use of fresh or lyophilized plasma. The use of dextran (Dextran, Expandex, Gentran) solutions in the treatment of burns is not necessary and probably not warranted, for experiments in our laboratory have revealed only detrimental effects attributable to dextran administered after burns.[6] Some improvement in length of survival of burned dogs could be shown when dextran was given in sodium chloride injection as opposed to no treatment at all. However, the use of saline solution alone gave a better survival record than the use of dextran in sodium chloride injection. The administration of dextran in water for injection was attended by poorer survival time than that shown by the group given no treatment.

TABLE 7.—*Parkland Mortality Expectancy Derived from Probits**

Burn Area, % Body Surface	1944-1947† Probit Y = 0.630 + 0.099x‡	1947-1951§ Probit Y = 1.683 + 0.067x	1952-1956‖ Probit Y = 1.71 + 0.050x
20	0.01	0.02	0.01
30	0.08	0.09	0.04
40	0.35	0.26	0.10
50	0.72	0.51	0.21
60	0.94	0.76	0.39

* 1.0 = 100% mortality.
† Plasma only; data from Moyer[2]
‡ % Body surface.
§ Blood-saline; data from Moyer.[2]
‖ Saline only; all deaths included; patients less than 61 years of age.

Guides to Use of Electrolyte Solutions: We wish to establish (by the preceding discussion) that the essence of safe treatment for shock that attends burns is the replacement of the extracellular fluid losses. A balanced salt solution resembling the ionic composition of extracellular fluid can be given by mouth or by vein. Only 81 of 142 patients who were hospitalized for treatment of burns required intravenously administered supplements of the oral intake in order to control shock. Some patients with burns that involved up to 60% of body surface were effectively treated by oral ingestion of salt water only. The ingested solution contained 3 Gm. of sodium chloride with 1.5 Gm. of sodium bicarbonate per liter of water (Moyer's solution). The container was placed in a pan of ice at the patient's bedside, so the solution remained chilled. The volume of fluid consumed depended on the patient's wishes to drink. The management of the fluid losses after most thermal injuries is made easy, safe, and effective by simply offering the patient a weak salt solution to drink as desired. The only patients in our series who were denied oral ingestion were in peripheral vascular collapse, were vomiting, or had acute gastric dilatation.

TABLE 8.—*Mortality from Thermal Injury**

Burn Area, % Body Surface	U.S. 1944-1952† Burned, No.	Died, No.	Mortality, %	Parkland 1952-1956‡ Burned, No.	Died, No.	Mortality, %
15-24	127	2	2	65	1	2
25-34	66	5	8	17	1	6
35-44	47	12	28	23	0	0
45-54	20	10	50	7	1	14
55-64	25	20	80	7	4	57

* All deaths included; patients less than 61 years of age.
† Combined series of patients with [illegible] by Moyer and were treated in St. Louis at St. [illegible] Homer G. Phillips Hospital; in Kankakee, Ill. at Kankakee Clinic, and in Dallas, Texas, at Parkland Hospital, 1944-1952; blood-saline-plasma series.
‡ Saline solution only.

To those patients who require intravenous replacement, the infusion of lactated Ringer's injection should be given as rapidly as necessary to overcome the symptoms of peripheral vascular collapse. The assessment of the circulatory status requires complete appraisal of the patient. Often the blood pressure cannot be measured by the sphygmomanometer because the extremities are burned. Even when the blood pressure can be recorded, it alone does not reliably indicate the presence of inadequate volume flow of blood; consequently, the functional alterations of the central nervous system, kidneys, heart, gastrointestinal tract, and sympathetic nervous system, as well as flow through visible peripheral vessels, are the indexes of inadequate circulation which must be used as guides to treatment. No formula of treatment can supplant observations of these functions of the patient. In order that trends can be seen, the observations must be made repeatedly. One looks for cool skin and pallor, with slowing of capillary return rates in unburned areas; empty peripheral veins, decreased arterial pulse volume, and increased pulse rate; diminished intensity of heart sounds, with a soft aortic second sound; excitement, thirst, restlessness, irritability, and disorientation, or sudden weakness, apathy, and decreased peripheral sensation; slowing of urine flow rates; and the presence of nausea or vomiting. When these signs are present, additional water and salt replacement is needed, regardless of blood pressure level. When these signs are abolished by treatment, the rate of infusion can be slowed, even if blood pressure has not returned to normal.

The hemoglobin and hematocrit levels should not be used as primary guides to the volume of fluids required, because the symptoms of circulatory failure are often alleviated long before the hematocrit level returns to normal. If one persists in treatment in order to lower the hematocrit level, a dangerous fluid overload may be imposed.

In retrospect, the volumes of salt solution administered have varied predominantly with the size of the patient and the extent of his burn. By colligation of these factors, a rough relation can be derived; that is, for each 1% of body surface burned, 1% of the calculated extracellular fluid volume needs to be replaced. Burns involving 20% or less of the body surface usually do not require treatment of hypovolemia. The fluid deficits attending burns up to 35% of body surface are usually replaced adequately in the first day or two exclusively by the oral ingestion of the sodium chloride-bicarbonate solution. As an example of the fluid and electrolyte therapy required for a burn of 50% of the body surface in a man weighing 60 kg. (132 lb.), about three to four liters of lactated Ringer's injection may have to be given intravenously in the first 6 to 8 hours and another two to three liters within the next 16 to 18 hours. During this time, the burned person is permitted to drink a hypotonic salt solution. If large volumes of salt solution are consumed, the signs of fluid deficiency may be alleviated, and the intravenous requirements can be reciprocally reduced.

No plain water should be offered to the patient during this first day, for it will be taken in preference to the salty water. If large quantities of plain water are taken, the state of shock is not modified, and the retention of water that ensues causes a progressive dilution of the body's salt. The reduction in osmotic concentration is often attended by signs of increased intracranial pressure, and it may lead to frank water intoxication, with scanty urine flow. This state has been confused with burn "toxemia," but it can be specifically treated by the infusion of hypertonic sodium salts and withholding water.

If the burn is extensive and shock has been present during the first 24 hours, the oral ingestion of salt solution should be continued for another 24 hours. In those patients with extensive burns, some infusions of lactated Ringer's injection may also have to be given the second day. On the other hand, the patient with a burn of about one-third of his body surface or the patient with a burn that has not been associated with evidence of hypovolemia will probably not require the ingestion or infusion of salt solutions after 24 to 36 hours. When salt water is drunk exclusively for three days after a burn, a high serum sodium concentration develops, even though the solution drunk was hypotonic (0.45%). This electrolyte aberration is more likely to occur in hot weather in children and probably stems from the inability of the kidneys to concentrate salt in the urine and thereby to liberate sufficient plain water from the ingested saline solution. The insensible losses of plain water take place at accelerated rates through burned skin,[7] and more especially when the body temperature is elevated. When the serum osmotic concentration is elevated, the patient shows the signs of need for water, such as thirst, fever, dry mouth, small volumes of urine with high specific gravity, and perhaps disorientation. This state too is sometimes not clinically differentiated from burn "toxemia," but, when recognized, it can be definitively corrected by the administration of water.

When salt solution is administered at adequate rates and the signs of shock persist or recur, a frequent cause of the refractory shock has been found to be acute gastric dilatation. The distended stomach is sometimes visible as epigastric fulness, but nearly always gastric tympany can be percussed over a larger area than normal, and extending farther cephalad. These signs are attended by grunting respiration and effortless vomiting or nausea with epigastric discomfort. The treatment is to forbid any oral intake and to empty the stomach with a nasogastric tube. The reflex vascular collapse is relieved when the distended stomach is decompressed.

Another less frequent cause of shock refractory to volume replacement is hyperthermia. Body temperatures of 104 F (40 C) and above have been encountered in burned patients when compression dressings were used, especially in the summer. Hypotension and other signs of vascular collapse often attend the hyperpyrexia, but recovery from shock follows the reduction of body temperatures accomplished by immersion of the patient in ice packs.

Alleviation of Pain

Often the immediate concern in the treatment of a burned person is the alleviation of pain. Pain is adequately and promptly relieved by the intravenous injection of morphine sulfate or meperidine (Demerol) hydrochloride. Analgesia, not sedation, is the objective of medication, for signs of central nervous system dysfunction are valuable guides to the adequacy of treatment for shock and to detection of airway obstruction or other ventilatory defect. The amount given should be determined by the patient's response to a slow intravenous injection. Much less than the regular dosage of analgesic is required for pain relief in burns because the drug is given intravenously, because the patient in shock is unduly sensitive to the effects of analgesics and depressants, and because the patient often experiences less pain from the burn than is anticipated. As determined by the patient's subjective response, 8 to 10 mg. of morphine sulfate administered intravenously often gives relief from pain. Much of the agitation and restlessness of the burned patient is interpreted as being due to pain, but actually it is behavior characteristic of the influence of anoxia. Commonly, the anoxia that occurs prior to treatment is incident to diminished cerebral blood flow, and the specific treatment of this apprehension is not morphine but rather fluid volume replacement and oxygen by mask. After the first few hours and when there is no evidence of circulatory insufficiency, the burned patient is ordinarily not in pain and not restless. Opiates can regularly be withdrawn at this time.

Measures Against Infection

Antibiotics are given parenterally for the first three or four days and then withdrawn until subsequent débridement is performed or until there is evidence of infection. Penicillin and streptomycin are commonly used for this initial period. The incidence of infection of the burned area has been little altered in our experience, despite frequent changes in our policy regarding the type, dose, route, and duration of antibiotic administration. Surface infection probably cannot be prevented by the use of systemic or topical antibiotics, but early systemic invasion by hemolytic organisms is effectively curtailed, as a rule, with penicillin given parenterally. The topical application of chemotherapeutic or antibiotic agents is futile in treating or preventing serious systemic infection, may be harmful by inducing sensitization, may allow the later emergence of antibiotic refractory organisms, causes maceration of the burned surface, and prevents dry eschar formation.

A tetanus toxoid booster dose should be given to patients who have been previously immunized against tetanus, and the opportunity to start active immunization should be taken in those who have not been previously immunized. Although active immunization will not prevent the development of tetanus early in the course of the burn, it may be of value in prevention of tetanus when repeated débridement and late reconstructive procedures are done. Passive immunization with antitoxin is not reliably effective in preventing tetanus with the usual 1,500 units, or even with 3,000 or 5,000 units. These and larger doses of antitoxin are attended by serum sickness, other severe allergic complications, and, occasionally, by anaphylaxis and death. The large doses with a high incidence of untoward reactions are not warranted unless the burn is excessively contaminated with material likely to contain Clostridium tetani.

Some recent immunological and experimental data suggest that treatment directed against a burn toxin may be beneficial after thermal injury, despite repeated failures over many years to identify and isolate the toxin. Immune serum globulin and convalescent burn serum have properties which extend survival times when given to burned animals. The benefits of these substances and the question of freedom from dangerous reactions in the patient are not sufficiently established to warrant their use in burns in man.

Local Treatment

The local treatment of burns should be simple and free from ritual and should consist only of exposure to air. No immediate débridement is done, and no washing or scrubbing is done. Blisters are left intact unless they are large and obviously subject to early rupture; then they are aspirated with a fine needle. If gross contamination is present, the foreign particles are removed. The patient is then put in bed on sterile sheets, and a cradle is put over him. The cradle is covered with clean sheets. If the burn is confined to either the dorsal or the ventral surface, the patient is placed with the side of the burn upward. If the burn is circumferential, he is frequently turned, so the deep burns will form a dry eschar and the weeping areas will crust. The dry eschar of the burn is relatively impenetrable to bacteria as compared to macerated burned skin.[8] Soaks and topical applications are avoided.

Two complications of dry, contracted eschars must be promptly treated when they are recognized. Occlusion of the vessels of extremities may occur incident to the tightly constricting, leathery envelope of a deep circumferential burn of the arm or leg. The burned skin functions as a tourniquet. Ischemia of the digits and distal extremity may be recognized early by the presence of hypesthesia or by complete loss of light touch perception in unburned areas, even though pinprick may still be felt. The constrictive effect of the burn can be relieved by long linear incisions through the depth of eschar along the long axis of the extremity. The incisions can be made without anesthesia, since constricting eschars are produced by full-thickness burns which are insensitive. If edema of the muscles is severe, the deep fascia may also have to be incised over each muscle compartment. Ordinarily, however, incisions through the dermal burn only allow the subcutaneous tissues to protrude and relieve the tension.

When the chest or upper abdomen is circumferentially burned, severe respiratory restriction develops as a result of the inelastic girdle of burned skin. Respiratory excursions are shallow, tidal air is low, and carbon dioxide is retained. With severe restriction, the tidal air is little greater than the physiological dead space, and the burned patient becomes progressively asphyxiated. Death may occur in such instances by reason of the local effects of the burn, which, if incurred on another part of the body, would have been nonfatal. The garroting effect of circumferential chest burns can be relieved and lives can be saved if bilateral incisions are made vertically through the burned skin in the anterior axillary line. The incisions should extend down across the costal margin on to the abdominal wall, if the deep burn involves these areas. Immediately, the incised wound separates, and the liberated chest expands fully, with inspiration.

Treatment of Bronchopulmonary Complications

Tracheotomy is frequently required in the early management of burned patients with attendant respiratory problems. By means of clinical observations, autopsy findings, and experimental data, it has been shown that a respiratory defect, resulting in arterial desaturation associated with pulmonary congestion and decreased elasticity of the lungs, is a characteristic of thermal injury. If whole blood or colloid solutions are used to control shock, respiratory insufficiency may be exaggerated, and, occasionally, in patients with extensive burns (regardless of type of therapy for shock), the respiratory difficulty is progressive.

The first clinical evidences of these changes in the lung are delayed several hours and consist of an increased rate of breathing and tachycardia; then the expiratory phase of respiration becomes active and labored. Finally, inspiration is difficult, and interspace retraction can be seen; usually, by this time, there is gross evidence of arterial desaturation. Surprisingly, moist rales may not be heard, but usually auscultation of the lungs reveals an increased bronchial quality to the breath sounds, whereas vesicular breathing is absent in scattered areas. Sibilant rales are characteristically heard during expiratory effort.

Tracheotomy should be performed, and a cuffed tracheotomy tube should be employed in order to use intermittent positive-pressure breathing during the inspiratory phase. If this treatment is begun early, the changes in physical properties of the lungs may not be irreversible, and the congested state is alleviated along with an improvement in elastic compliance.

Another indication for early tracheotomy is for the treatment of burns of the upper respiratory passages. Mucosal burns on the tongue, mouth, or pharynx are evidence that tracheotomy will probably be required. If the patient is hoarse when first seen or becomes hoarse in the next few hours, tracheotomy should be performed immediately, in order to obviate more complete airway obstruction which nearly always follows hoarseness.

Tracheotomy is often necessary when the victim has inhaled noxious gases and smoke. There may be no signs of mucosal burn, but hoarseness is often present, coarse rhonchi and wheezes appear early, cough is frequent, inspiratory effort develops, moist rales and atelectatic areas occur, and frank pulmonary edema supervenes. These signs and their mode of progression serve to differentiate this laryngotracheobronchiolitis from the previously described pulmonary congestive state that may attend burns not directly affecting the respiratory passages. After performance of tracheostomy for burns of the respiratory passages or for inhalation of irritant gases, constant warm mainstream nebulization of water directly into the tracheotomy tube is necessary. These states are frequently fatal, but the use of anti-inflammatory steroids favorably modifies the pulmonary response to direct thermal injury. The addition of mucosal shrinking agents such as phenylephrine (Isophrin, Neo-Synephrine) hydrochloride to the nebulized water is beneficial in reducing frictional resistance to airflow. Intermittent positive-pressure breathing is usually required.

Another type of pulmonary injury, traumatic wet lung, is incurred with burns when explosion attends conflagration. Characteristically, there is an interval of many hours between the injury and the onset of cyanosis, with pulmonary edema. If one can anticipate the onset of this state from the history of explosion and by subtle evidences of pulmonary congestion, the performance of tracheotomy and the use of intermittent positive-pressure breathing can prevent death.

Miscellaneous Adjuncts to Treatment

The indications for use of gluco-corticoids (corticosteroids) in burns are probably limited to prevention of inflammatory response in the tracheobronchial tree after inhalation of smoke and other irritating gases and replacement therapy for those who have adrenocortical suppression as a result of previous steroid treatment.

Lowering of the body temperature has been suggested to have a favorable influence on severely burned persons, but we have been unable to demonstrate that over-all mortality is any different in hypothermic animals after a standardized scald than it is in normothermic controls. However, the hypothermic dogs lived longer.[9] Our preliminary experience with hypothermia in burned man indicates that it may be palliative but not definitively helpful.

Summary

The state of shock that attends thermal injury can usually be successfully and safely treated by balanced salt solutions given by mouth and vein. The use of whole blood and plasma in the first 48 hours after a burn is usually unnecessary and often harmful. Respiratory insufficiency commonly attends burns, and, usually, it requires the performance of a tracheotomy for adequate treatment. Incision of the eschar of a burn on the chest will, at times, relieve ventilatory inadequacy. Analgesics should be given intravenously in small doses and discontinued early in the course of the burn. The local treatment consists of exposure of the burn. Longitudinal incisions through the eschar of a burn on the extremities may be required to relieve the vascular occlusion incident to circumferential contraction of the burned skin. Antibiotics should be given systemically for three or four days after thermal injury, then withdrawn until specific indication for their need arises.

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FLUID REPLACEMENT IN SHOCK AND HEMORRHAGE

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The purpose of this presentation is to present briefly the fundamentals of resuscitation after injury or operation and to discuss, within this framework, the current frontiers of investigation and treatment.

After hemorrhage, the body's compensatory mechanisms are able to maintain a normal blood pressure until approximately 20% (1,000 cc.) of the blood volume has been lost. About this point the pressure begins to fall and by the time 40% (2,000 cc.) has been lost, the pressure becomes imperceptible. These estimates refer to acute hemorrhage. Chronic blood loss is much better tolerated, but acute blood loss, in the chronically ill patient whose blood volume is already contracted, is tolerated poorly.

Agents Used in Replacement Therapy

The primary principle of replacement therapy is that the volume be replaced immediately in order to maintain the circulation and the exchange of oxygen and carbon dioxide as well as other essential substances. The preferable fluid is blood of the patient's own type, which is now available in almost every operating room in the United States. Since obtaining cross-matched blood requires time, it is not always available in the accident ward emergencies. What can be used while blood is being cross matched?

The experience in Korea demonstrated the feas
bility and desirability of using type O blood co
taining a low titer of isoagglutinins. This blood w
used without cross matching and without regard
Rh type. Thousands of units were administered, an
the policy proved sound. Within moments of a
mission, a casualty could be receiving one or mo
transfusions. Civilian practice, with its problems
hemorrhage during obstetrical labor as well as
those patients who have previously been transfuse
requires additional care as to Rh compatibility.
has proved quite feasible, however, to maintain
the emergency room and in the obstetrical and s
gical suites two bottles of type O blood, low tit
Rh negative, for use in emergencies until cr
matching has been achieved.

It cannot be overemphasized that blood is
preferable solution for replacement after hem
rhage. When blood is not available because
inadequate planning or unusual circumstanc
compromises are essential. The volume of blood
more important than is the concentration of
blood cells. Normal human plasma is the most u
ful alternative, and it should always be availa
for instant use if type O blood is not on hand.
fact that there was a surplus of dried, inexpensi
conveniently available plasma left over from Wo
War II spoiled the persons in charge of the bl
banks. When the hepatitis virus made the use
this plasma impractical (plasma prepared from

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of 50 blood donors), the blood bankers tended to say that plasma was not good and, therefore, was unavailable. Plasma from single donors may be a bit troublesome to prepare, but its hepatitis risk is no greater than that of blood, and its shelf-life is much greater. On the basis of work by Allen[1] and others, which demonstrated that prolonged storage (six months) of plasma at room temperature would sterilize plasma of its hepatitis virus, the National Research Council has co-ordinated a national study of means of sterilizing plasma with heat. At present, these studies indicate that heating plasma to 60 C for 10 hours inactivates the hepatitis virus. The process, however, results in the loss of fibrinogen and in other changes in the plasma proteins. Nevertheless, studies at the time of this writing suggest that a useful modified plasma solution may result from this or from chemical sterilization.

A number of medical centers now recommend that immune serum globulin be administered to patients receiving multiple blood transfusions in an effort to prevent hepatitis. Statistical evaluation is not yet complete as to its efficacy, but, with an incidence of hepatitis carriers of 1 in 250 blood donors, such efforts seem well placed.

Concentrated normal human serum albumin (Albumisol, Normal Human Serum Albumin) remains available through the Red Cross, but it is not easily obtained because of its cost. However, it provides excellent expansion of the blood volume and, in the entire history of its use, only one patient has proved sensitive to the albumin. The latter record is unique since some patients with nephrosis have received hundreds of infusions of albumin.

Dextran (Dextran, Expandex, Gentran) in 6% sodium chloride injection has now been used for a decade as a plasma volume expander. It has proved useful, and few emergency rooms can function optimally over a prolonged period without dextran. Since its shelf-life is several years, a supply can be maintained in the emergency room with little difficulty and at modest cost. The national stockpile of dextran is now several million units.

There is no arbitrary limit to the amount of plasma expanders which can be used. Their use always connotes a pressing need and a lack of the specific blood or plasma fraction. The amount to be given can only be titrated against this need. Experience indicates that the first one or two units administered are almost entirely safe and without danger of the development of any bleeding tendency in the patient.

When the aforementioned preparations are not available, sodium chloride injection should be administered, but its usefulness as a volume expander is limited.

Specific Problems

The problem which confronts the surgeon today is not what to give to replace blood volume deficiency; the problem is what to give after the blood volume has been restored. In most patients, no major problem persists. In a few, shock remains refractory or acute renal failure threatens. How can these problems be met?

First, how can we prevent acute renal failure? The only preventive method which has been found effective is to minimize the degree and duration of shock by restoring blood volume and, thereby, to restore the competence of the renal circulation. Neither hydration, diuretics, nor sympathetic nerve blockade have yet been demonstrated as being useful in preventing this dreadful complication. The metabolism of hemoglobin does not appear to be a causative factor, although transfusion reactions quite obviously result in a moderate degree of acute renal failure.

A number of studies have been reported recently pertaining to the treatment of refractory shock. Stirman and colleagues[2] have reported that, in dogs, sodium chloride injection lowers the mortality after replacement of blood. Others[3] have indicated that hydrocortisone (Cortef, Cortril, Hycortole, Hydrocortone) is of value, but this has not been confirmed in our laboratory, nor has it met our clinical need. Lillehei[4] has indicated that hydrocortisone and also autonomic blocking agents will lower the mortality in experimental shock due to bacteremia.

The role of vasoconstrictors remains controversial. From the laboratory, Webb[5] has currently reported the relative benefits derived when treating hemorrhagic shock in dogs. Lillehei failed to find any beneficial results from the use of vasoconstrictors in the treatment of septic shock.

In Korean experience and in civilian practice, the young man does not appear to benefit from vasoconstrictors. So far, in the resuscitation of thousands of injured young people, there has not been one whose life appeared to have been saved by vasoconstrictors. This does not seem to apply to the geriatric group. In the latter group, the coronary arteries and the cerebral arteries may be rather rigid and partially occluded by atheromatous plaques. Blood flow may be minimal, and a fall in blood pressure may prove catastrophic. A recent review[6] was made of those patients in our clinic who had suffered a cardiac infarction or a cerebrovascular accident during the 30 days after operation or injury. These patients were chiefly in the older groups. Nineteen patients had a myocardial infarction, 15 (79%) of which had occurred within the first week after operation. Half of these occurred on the day of operation or within 24 hours thereafter. Eleven patients had had cerebrovascular accidents, and these complications had their onset distributed equally throughout the first three weeks. Further review revealed that the patients with myocardial infarction had undergone varying periods of operative hypotension.

A similar clinical experience has resulted with acute renal failure, after resection of aortic aneurysms. For these reasons, vasoconstrictors, in conjunction with blood transfusions, may be indicated in the management of the older patients.

Finally, the blood pressure, refractory to multiple transfusions, may occasionally respond dramatically to the intravenous injection of 1 or 2 Gm. of calcium gluconate.[7] Presumably, this is due to an increased cardiac output which occurs as the concentration of ionized calcium is raised.

Summary

The treatment of shock after operation or injury consists primarily of restoration of blood volume with whole blood. Expedients and clinical evaluations of supplementary therapeutic measures may be superimposed, but the one fact remains paramount: The systemic ischemia and anoxia which result from traumatic shock is a major, continuing injury in itself. Every effort must be expended to prevent its occurrence, minimize its magnitude, and shorten its duration. The deleterious effects of this secondary insult are more disastrous than are the local effects of the primary injury.

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EMERGENCY CARE OF WOUNDS

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Unfortunately, wars have provided the greatest stimulus to advances in the treatment of wounds. Between wars, the basic principles of emergency treatment are frequently forgotten or are overlooked and have to be relearned at the expense of increased morbidity and mortality in the early phases of a new war.

Medical officials of the 15 North Atlantic Treaty Organization (NATO) nations recognized the need for documenting lessons of World War II and the Korean war. They, therefore, authorized the publication of a NATO handbook entitled, "Emergency War Surgery." It represents contributions of international experts who saw wounded soldiers at the front. The first draft was submitted to medical authorities of all 15 NATO nations as well as to 40 American surgeons with wartime experience, who generously offered criticism. The United States and Canadian issues have been released within the past year. Surgical principles contained in this volume are just as applicable at the local hospital as at the war front. With the prayer that this volume may never be required during war or mass casualties, I commend it to your use for the treatment of wounds encountered in peacetime.

Early Emergency Measures

Death of the patient within moments after a gunshot wound is usually due to gross hemorrhage, to destruction of vital centers, or possibly to asphyxia. Even though the person appears to be dead, possibilities of resuscitation should not be overlooked. Clearing of the airway followed by artificial respiration with the mouth-to-mouth method, cardiac massage, or pressure transfusion by the arterial route might effect resuscitation in rare cases. If the patient is alive when first seen, certain surgical measures may have to be applied immediately, if he is to survive long enough for resuscitation and later necessary surgery. Foremost among the early measures are assurance of an adequate airway, the control of hemorrhage, if possible, and restoration of the circulating blood volume. Perhaps next in importance are occlusion of a sucking chest wound, release of tension pneumothorax, or the performance of a tracheostomy in impending asphyxia. If a patient survives the hazards of hemorrhage, asphyxia, or a serious cardiopulmonary imbalance, he then becomes a candidate for reparative or restorative surgical procedures. The patient's survival, beyond these measures, still is threatened by infection and by delayed physiological alterations. Among these late causes of death are delayed and so-called chronic shock due to the absorption of toxic products from necrotic tissue, which remains as a result of nonrecognition of devitalized tissues and inadequate débridement, severe electrolyte imbalance, and protein deficiencies. If these complications are to be held to a minimum, early resuscitation and surgical management must be in keeping with well-established surgical principles.

While resuscitation is being carried out, the surgeon should make a rapid appraisal of the extent of injuries and should determine which surgical procedures are of the highest priority. On occasion, in spite of the most heroic measures to overcome shock due to hemorrhage, failure of resuscitation may be due to continued bleeding within the chest, the abdomen, or other areas not controllable by tourniquet. Under these circumstances, the surgeon is forced to operate in an attempt to control the hemorrhage. The bleeding vessel should be secured through the most direct incision and with a minimum of trauma or other surgical procedures. Clamping of a large bleeding vessel will frequently result in a rapid improvement of the pulse and blood pressure, thus making resuscitation possible. Only after this has been accomplished may other indicated surgical procedures be carried out.

I can not emphasize too strongly the necessity for adequate refilling of the vascular tree, whether blood, plasma, or plasma expanders are used. Amounts must be given in such quantity as to restore systolic blood pressure to a minimum of 80 mm. Hg, preferably 100 mm. Hg before operation. During World War I, blood transfusions were rarely given. During World War II, the supply of blood was usually adequate on most fronts, and, on occasion, blood or plasma was given in large amounts. Not until the Korean war was it discovered that a single patient might require restoration of blood volume in amounts not only equal to his estimated blood volume before wounding, but, in some cases, in amounts even double or triple the estimated blood volume.

Estimation of Extent of Injury

In my opinion, the most important single factor in estimating the extent of damage due to gunshot wounds is knowledge of the type of weapon and the missile producing the wound. Although the size of the missile is of some importance, the velocity with which it is propelled is of the greatest importance. Stated in its simplest form, the amount of energy imparted to the body by a missile is derived from a formula in which the mass (the weight of the missile) is multiplied by the velocity squared. For example, before World War II, our military rifle fired a 30-caliber projectile at an estimated muzzle velocity of 2,300 foot-seconds (ft.-sec.). If all of the energy from this missile were transmitted to the tissues of the body, the estimate would be based on multiplication of the weight of the 30-caliber missile with the factor of 2,300 squared. Before the war, we had knowledge that the Japanese were developing a 25-caliber missile, which was projected at a muzzle velocity of 5,000 ft.-sec. It is immediately apparent that the weight of this missile is relatively unimportant when we consider multiplying that weight by the factor of 5,000 squared. Thus, the amount of energy imparted to the tissue determines to a great degree the amount of injury. On this basis, it is apparent that wounds produced by low-velocity weapons will cause little tissue damage remote from the track of the missile or weapon itself. For this reason, one of the simplest of wounds would be that produced by a knife or bayonet. Unless transection of a major vessel threatens life immediately, adequate inspection of the wound to its depth will disclose all of the injury present, and the surgical principles applied would be those dealing only with the local damage. Even high-velocity missiles, if fired from a great distance, may be practically spent when striking the body, and the amount of tissue damage may be minimal. This may be comparable to the amount of tissue damage produced by large or even small fragments, such as shell-casing fragments, if also projected a considerable distance. Such fragments, however, produce massive wounds and may produce tissue damage quite remote from the track, if the person is in close proximity to the explosion. Although the missile from a revolver may be equal to or larger in size than the average rifle missile, the velocity at the muzzle of a revolver is much less than that of the high-powered rifle. It is apparent, then, that the velocity of the missile and the proximity of the person to the wounding weapon become exceedingly important. Practically every conscious patient is able to describe the nature of the weapon, and the surgeon should anticipate the extent of tissue damage remote from the wound tract.

Importance of Adequate Débridement

In World War I, surgeons failed to recognize that tissue was damaged for many, many centimeters remote from a missile track. Wounds were inadequately débrided, in that devitalized tissue was not removed. Under these circumstances, primary closure of the wounds resulted inevitably in infection as well as the retention of necrosing tissue, which, because of its toxic effects, resulted in complications or death at a later time. This same principle applied when amputations were performed at or near the wound tract. Days after amputation, necrosis of tissue took place in the stump, and primary closure was out of the question. For this reason, the so-called guillotine amputation was the amputation of choice during World War I.

Even in the early days of World War II, débridement was woefully inadequate. Surgeons soon learned that boldness was essential and that the entire wound had to be exposed. Such an approach revealed, to a startling extent, the amount of devitalized tissue deep in the wound. In carrying out a débridement, devascularized skin should be excised, and all muscle that does not respond by contraction to pinching by a forcep should be removed. All viable bone should be left in place; in fact, large detached fragments of bone should be thoroughly cleansed and replaced in proximity to viable bone. Damaged nerves should not be débrided and should not be repaired at initial surgery. The site of nerve damage should be carefully described in the record, in order that later nerve repair can be carried out.

Perhaps the most important surgical advance during the Korean war was the application of proper principles of débridement to major blood vessel damage. Surgeons trained at the Vascular Surgical Center, Walter Reed Hospital, were sent on special missions to the Korean front for the primary purpose of restoring the continuity of damaged major blood vessels in those wounded. In the first series of cases, in addition to excising all portions of a major blood vessel obviously damaged, the ends of the vessel (which appeared normal to the naked eye) were further resected. One centimeter of apparently normal vessel was removed from both the proximal and the distal end of the resected vessel. Microscopic examination of these segments showed, in every instance, damage to the intima, which, inevitably, would have led to thrombosis and failure. This, then, explains the failure of attempts to repair or to bridge damaged major blood vessels among the casualties during World War II. Damage to major blood vessels in the patients' extremities, both in World War I and World War II, resulted in an average amputation rate of 55%. At the Korean front, application of this single principle, together with the use of grafts to bridge wide gaps in a patient's major blood vessels, cut the amputation rate down to slightly less than 12%.

In carrying out débridement, after all devitalized tissue has been removed, care must be taken to cover denuded bone, nerve, or major blood vessels with muscle. This should be done, even if muscle groups need to be temporarily transposed to effect adequate coverage. Such wounds should never be closed primarily. The high rate of infection precludes such a procedure. After 7 to 10 days, secondary closure is performed. There are certain exceptions to this rule; for example, in the débridement of wounds of the skull, dura, or brain, the dura should be closed tightly, even if substitutes need to be used. The scalp and the skin on the face, because of a generous blood supply, may be closed primarily. It also is evident that wounds of the chest wall should be closed in order to prevent sucking. The abdominal wall should be closed tightly, except for drainage or exteriorization of large intestine, both being through separate incisions. In open wounds of the chest wall, one emergency procedure which has been valuable is the temporary closure with a series of towel clips, after which cleansing and indicated surgical measures might be instituted more leisurely.

General Principles of Wound Treatment

In addition to paying great attention to exploration of wounds to their depths, so that adequate débridement might be carried out, one should remember that missiles, especially those fired at high velocity, may travel great distances within the body. By following fascial planes, missiles entering the buttocks might ultimately lodge in the abdominal cavity or even traverse the diaphragm and produce damage within the chest. When a wound of exit exists, sighting along the line between the wounds of entrance and exit may give a rather faithful indication of the areas damaged, but the bizarre traverse of some wound missiles should lead one to suspect damage remote from the estimated missile track. This factor is especially important in that wounds of the abdomen or of the chest may involve both cavities.

In wounds of the neck, one must respect the multiplicity of organs and, therefore, be prepared to deal with injuries of the pharynx, trachea, or upper esophagus, as well as major blood vessels. It may be necessary to open the upper chest in order to secure great vessels of the neck at the points of origin. Care should be taken, wherever possible, to secure airtight closure of wounds of the trachea or esophagus. Even when this is possible, drainage must always be instituted. Tracheostomy should be performed if the surgeon suspects that it might be required. In other words, if a wound is such that one even considers the probability of tracheostomy, that alone is sufficient to warrant a tracheostomy. Even if the conditions present at the time of surgery would not seem to warrant tracheostomy, it is well to remember that later complications may demand it at a time when facilities may not permit an emergency procedure.

With reference to the hand, only that tissue which is obviously damaged beyond recovery should be removed. Every shred of tissue should be retained for future reparative surgery.

As a rule, wounds of the chest cavity, sufficient to lacerate or transect great vessels or chambers of the heart, result in death before the surgeon reaches the patient. It was well demonstrated during World War II that wounds of the chest should be treated conservatively. Sucking wounds, of course, should be closed and the possibility of tension pneumothorax should never be overlooked. Repeated aspirations of blood from the chest cavity usually suffice, though, on occasion, hemorrhage can be controlled only by thoracotomy.

Wounds of Solid Viscera

Wounds of the spleen, whether of the spleen itself or of the splenic pedicle, require splenectomy. In liver injury, detached or devitalized portions are removed. Whereas superficial lacerations may be sutured, deep lacerations require packing, especially to control hemorrhage. Adequate drainage must be established; drains should not be removed early, because collections of bile may become loculated. Injuries to the pancreas are serious. Lacerated or fragmented portions of the tail or body of the pancreas should be removed. Injuries to the head and the major ducts of the pancreas are usually fatal; even adequate drainage may not be effective in preventing widespread necrosis from pancreatic juices. As more experience was gained in World

War II and in the Korean war, a more conservative approach was used in wounds of the kidney; control of hemorrhage, suture of the kidney substance, packing, where necessary, and routine drainage of the kidney area were effective in salvaging many kidneys of patients.

Wounds of Hollow Viscera

Throughout the length of the digestive tract, from the nasopharynx to the cecum, all wounds should be closed by primary suture. This may, of course, require resection of portions of the stomach and, especially, of the small intestine. It is to be remembered that small lacerations of the intestine should be closed transversely in order to avoid constricting the lumen. This principle in the surgery of the digestive tract, however, does not apply to wounds of the colon or rectum. Regardless of the procedure carried out, it must include a colostomy. In those portions of the large intestine where mobilization makes it possible, the damaged portion may be exteriorized in the form of a colostomy. Care must be taken, however, to assure that an adequate section of the colon is exteriorized in order that the colostomy may be a safe one. In transection of the large intestine, the two ends of the intestine may be brought out through the abdominal wall. A great portion of the large intestine, and especially of the lower sigmoid and rectum, can not be mobilized. Even though it may be possible in many instances to carry out a primary repair at the site of injury, a colostomy must be performed in an area of large intestine proximal to the site of injury.

Certain portions of the gastrointestinal tract do not lend themselves well to exploration. Therefore, care must be taken to discover wounds of the posterior wall of the stomach or of the second and third portions of the duodenum. In wounds of the ureter, the ureter may be primarily repaired, but diversion of the urinary stream proximal to the site of injury and repair should be carried out. This principle applies also to injuries of the urethra. Though it may be possible to repair the urethra over catheters or sounds, the temptation to leave an indwelling catheter alone should be avoided. In these instances, a cystostomy should be performed. When the bladder is injured, care must be taken to close that portion of the bladder which is within the peritoneal cavity, and a cystostomy should be performed through the extraperitoneal portion. Other hollow viscera or tubes include the gallbladder, which, if damaged, should be removed. Major biliary ducts should be repaired over, or bridged by, a long-armed T-tube. Again it is important that adequate drainage be established.

Hazards of Postoperative Period

When large quantities of blood or blood substitutes have been required to overcome shock due to hemorrhage and, especially, after major surgical procedures have been carried out after resuscitation, it is well to remember that such patients may later go into shock. Often the amount of blood volume restoration, which has been adequate to carry patients through operative procedures, will be found to be inadequate in the postoperative period. In practically all injuries, there is a certain degree of vasoconstriction. Filling of the vascular tree in the presence of vasoconstriction, whether it be produced through reflexes of the autonomic nervous system or by the use of vasoconstrictor drugs, may lead to a false sense of security. When vasoconstriction is released, the amount of blood within the vascular tree may be inadequate, and the patient will go into deep shock. This situation frequently evolves, and shock becomes present even on such trivial movements as turning of the patient or transporting him from the litter to a bed.

Finally, one should never overlook the possibility of tetanus. Those patients who have been previously immunized against tetanus should have a booster shot. Those who have not had immunization should have protection by passive immunization during the period of recovery as well as later active immunization.

Comment

Over 31 years of my professional career were spent in the military service. A great amount of this time was spent in assisting surgeons from civilian life to perform surgery under military conditions. Included in this effort has been a major responsibility in the development of the NATO War Surgery Handbook. I can not leave the subject of the treatment of wounds without reminding all members of the medical profession of their grave responsibility in the case of war or, especially, of mass casualties. I personally believe that every physician should acquaint himself with at least the major principles delineated in the NATO document. He should be ready, willing, and able to participate in the care of mass casualties. The most experienced surgeon can contribute best in resuscitation, in appraisal of wounded, and in determining priorities of care. His supervision of less qualified surgeons will effect greater care to greater numbers. In the event of mass casualties, the nonsurgically trained physician, as well as the dentist and the veterinarian, should be utilized to care for burns, fractures, contusions, and lacerations, to débride soft tissue wounds, to control hemorrhage, and to perform resuscitation. Surgical procedures which require the training and abilities of the surgically trained specialists will require their services to such extent that the nonsurgically trained physician must be prepared to carry out all procedures short of major surgery within the abdomen, chest, neck, or head.

2101 Constitution Ave., N. W.

The NATO handbook, "Emergency War Surgery" may be obtained for about $2.25 from the U. S. Government Printing Office, Washington, D. C.

J.A.M.A., June 4, 1960

MANAGEMENT OF PATIENT WITH MULTIPLE INJURIES

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The patient with severe multiple injuries offers one of the most challenging problems in medicine, but unfortunately the injured patient intrigues only a few physicians. The management of patients with severe injuries is not only difficult but has also become unpopular. Great emphasis has been placed on lowering the mortality after major elective procedures. It is almost impossible to obtain valid mortality figures on patients with multiple injuries. It is so easy to think that the patient, after serious trauma, has sustained so much injury that he cannot possibly live, and, therefore, the death of such a patient does not prey upon the physician's conscience as much as the loss of a patient who walks into the hospital requiring an elective procedure for a large gastric lesion.

The injured patient is usually not in the upper income bracket or the upper social strata and therefore is not so appealing to the private practitioner. All physicians are extremely interested in the prominent older citizen who has a prostatic difficulty, but few are interested in the rowdy youngster who is admitted, partially inebriated, in the middle of the night, with a gunshot wound or multiple injuries after an automobile accident. Most injured patients are admitted in the midst of a busy day or at night, and it has become common practice to shift the responsibility of the severely injured to younger physicians on the staff.

The emphasis on research and teaching in the fields of cancer and cardiovascular disease has aided considerably in improving the treatment of these entities. The field of trauma has received less emphasis. The treatment of the injured patient is an emergency and may become the responsibility of almost any physician.

It is the purpose of this communication to reemphasize well-established techniques in the care of the patient with multiple injuries and to outline a type of organization for care, along with an explanation of the physiological principles involved. Each patient with multiple injuries presents a different problem; therefore, it is impossible to suggest a specific routine for all patients.

Immediate Care and Transportation to a Hospital

For the extensively injured there are no rules that will cover all cases, but there are certain guiding principles. Unlike many single-injury states, multiple injuries require two specific aspects of care: (1) priority of certain systems for treatment and (2) organization of a team of persons to carry out therapy. Either at the scene of the accident or in the emergency room of the hospital, several professional and lay persons will make up the group that goes into action to care for the patient with multiple injuries. Irrespective of the level of care, someone must take charge. This person should be the one with the most advanced experience and judgment. This leader is the most important factor in the organization of the care of the patient. He must assume full responsibility and dictate to the members of the team their specific tasks.

The first physician, whether he works at the scene of the accident, in a battalion aid station, in his office, or in an emergency room, carries a distinctive and heavy burden. He has the greatest opportunity to save life and limb. The physician who first sees the patient is not merely a first-aid man but an important member of the team who will resuscitate the casualty. The care that he gives is of an emergency type, but he must take time to institute procedures that will prepare the injured patient for transportation to the nearest hospital or for necessary surgical therapy. Hurried transportation to the hospital may lead to undue deterioration of the patient's condition during transportation. The importance of a short interval of time between injury and admission to the hospital is well recognized, but a slight delay for further restoration may be warranted because the patient may be better prepared to withstand the trauma of transportation. Emergency treatment at the scene of the accident should be the most complete care possible with the means available.

When an accident occurs and there are more than one injured, the patients must be sorted and cared for according to the urgency of their injury and the facilities available. The physician can usually tell with a quick glance the lifesaving measures that may be necessary immediately. The objectives of treatment should be, first, to stop the continuing insult of the wound and, second, to start restoration as soon as possible.

Maintenance of Adequate Respiratory Function.—The patient's airway must be kept open. Three to five minutes is about the limit before anoxia of the brain due to a plugged airway will produce permanent brain damage or death. Even if the obstruction is incomplete, the patient may not survive more than a few minutes unless the air passage is adequately opened. The patient should be placed on his side with the mouth open if he is unconscious. The operator's fingers may be covered with a handkerchief and used as a mouth gag. All foreign bodies should be removed, and the tongue should be pulled

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forward. It may be necessary to insert a safety pin through the tongue and attach it by a string to the clothing.

A sucking wound of the chest can be closed easily by a large bulky dressing. In some instances, it may be necessary to administer artificial respiration. Any one of several methods is useful. The operator should use the method with which he is most familiar. Mouth-to-mouth breathing is the simplest and very effective. The Holger-Neilsen procedure is familiar to many persons and is a highly effective method in providing adequate respiratory exchange. If a foreign body is lodged in the trachea, the patient may be encouraged to cough and expel it. After some injuries a tracheostomy is necessary.

Arrest of Hemorrhage.—After assurance of respiratory exchange, the next in priority is the arrest of hemorrhage. If hemorrhage is obvious externally, it usually can be stopped by the application of pressure directly over the bleeding area. Hemostats are convenient but usually are not necessary. The use of pressure points has been highly overemphasized, and it is doubtful if they are really of any value.

In general, tourniquets are to be condemned for use at the scene of the accident in almost all instances. It is rare that hemorrhage cannot be controlled by a well applied pressure dressing. In some unusual circumstances, however, it may be mandatory that a tourniquet be used to save life. If a tourniquet is utilized, it should be put on tight enough to occlude the arterial flow in the extremity. The most common difficulties with tourniquets are instability of the tourniquet causing loss of pressure, trauma to an underlying nerve, or compression insufficient to occlude arterial flow. If the tourniquet is applied with inadequate pressure or loosened after its application, it may occlude venous flow but not arterial flow and thereby cause greater loss of blood. When a tourniquet is applied, it should not be removed until the patient is in an institution and under the care of a physician who is prepared to deal with rapid major blood loss. Obviously, if the patient is bleeding from areas that cannot be controlled without an operative procedure, he should be transferred to the nearest hospital as rapidly as possible.

Preparation and Transportation to the Hospital.—It should be the initial physician's responsibility to put the patient in the best possible condition to withstand the further trauma of transportation to the hospital. After he has assured himself that there is adequate respiratory function and that hemorrhage has been arrested, other areas of injury should be attended. All fractures should be carefully splinted. If hypovolemia exists, an intravenous infusion of a plasma volume expander or an electrolyte solution should be administered during transportation to the hospital.

The importance of prompt admission to a hospital is well recognized, but preparation of the patient to withstand transportation may be more important. The commonest mistakes in care, prior to a patient's admission to the hospital, are inadequate splinting, overdosage with morphine, inadequate control of hemorrhage, and transportation without proper preparation.

Great attention should be given to the patient's position. If he is unconscious, he should be placed on his side or on his abdomen with his head turned to the side. If there is any evidence of injury to the spine, the patient must be kept on a rigid support, such as a door, with his face down; when this is not available, he should be placed face down on a blanket so that the spine is maintained in slight hyperextension. If there is any question of cervical spine injury, traction on the head should be exerted by an attendant.

When a burn is associated with other injuries, it should be covered with a clean cloth and intravenous administration of fluids started.

Great care should be exercised in the use of narcotics initially. In some instances such as major fractures, burns, and abdominal injuries, it may be necessary to give an opiate; however, patients who are unconscious or who have a head injury, airway block, or severe shock should not be given a narcotic.

Initial Hospital Care and Resuscitation

Initial care in the hospital should be a simultaneous appraisal of the patient's condition and the institution of necessary resuscitative measures. One physician, preferably a general surgeon, should take charge and direct activities. While he is making a cursory examination and obtaining a few aspects of the history of the injuries, other physicians may be drafted to start work or assist in maintaining a good respiratory exchange.

History.—The initial history may be a short one, but a few questions to the family or to someone who has accompanied the patient may reveal important aspects concerning the mechanism of injury and pertinent aspects of the history of the patient. A description of how the accident occurred may lead the physician to suspect certain injuries and thereby be able to perform a better examination. The circumstances surrounding the accident may be revealing as to the organ systems that might possibly be involved in the injury. Sometimes, of course, the patient is able to relate a good history himself.

Physical Examination.—Initially, a rapid examination should be carried out. It must be a general one but follow an orderly plan. It may be necessary to cut off the clothes with scissors rather than traumatize the patient further by removing them. Examination should be directed first to the areas of obvious injury, but an over-all, quick examination also should be carried out. The following outline is helpful.

General: state of consciousness, respiration, pulse, position of patient, color, and odor.

Head: palpation of scalp and cranium, inspection of ears and nose for hemorrhage or cerebrospinal fluid, palpation of facial bones for fractures.

Eyes: state of the eyeballs and pupils. Not infrequently there is serious damage to the eyes in patients sustaining multiple injuries, and these are often overlooked. It should be of prime importance to obtain, as accurately as possible, the visual acuity of the patient. This should be recorded for each eye separately. Certain lifesaving procedures would receive higher priority, but early consultation with an ophthalmologist may permit him to carry out procedures that would be of considerable benefit in the prevention of loss of vision.

Mouth: inspection for foreign bodies, bleeding, or loose teeth.

Neck: state of blood vessels, inspection for internal or external bleeding, rigidity, possible injury to the cervical spine.

Thorax: observation of respiratory excursion, palpation of rib cage, heart action.

Abdomen: examination for distention, rigidity, observation of movement, and evidence of penetrating injury or tenderness.

Genitalia: examination for urinary extravasation, mechanical injury, or hematuria.

Extremities: palpation for tenderness, deformity, pulses, action of joints, color, temperature, sensation, and movement.

Skin: inspection for wounds of all types, including burns or irritations from gases or chemicals.

Roentgenograms.—In most patients with multiple injuries, certain roentgenographic examinations are necessary; however, such examinations are overemphasized. For the extensively injured patient, there is nothing rational in ordering roentgenograms of all bones which examination shows might possibly be fractured. One must decide whether a roentgenographic finding may change the treatment in the next few hours for the critically ill patient or whether he should be disturbed as little as possible. The patient should be subjected to as little further trauma as is absolutely necessary. Rapid changes in position usually lead to a fall in blood pressure in a hypovolemic patient.

It is not uncommon that many unnecessary roentgenograms of the skull are taken early. Unless the patient is cooperative enough to hold his head quietly, roentgenograms of the skull should be postponed unless the physician in charge believes they are absolutely necessary to determine the presence of an open depressed fracture or a fracture at a site which could readily produce injury to the middle meningeal artery. The necessary roentgenograms should be taken immediately, but x-rays of questionable injuries should be postponed; however, the physician in charge should watch for the development of further symptoms and have the necessary films made later. An injury which at first seems apparently minor may give the patient the most trouble afterwards. This means that the management of the patient with multiple injuries is a continuing affair. The physician in charge must follow the patient until he has become stabilized after definitive care.

Records.—As soon as possible, the physician in charge should begin a record of the patient. This must include when the accident occurred, how it occurred, and where it occurred. The findings of the initial examination should be recorded, particularly the extent of vascular, nerve, and bone involvement, vision, blood pressure, and pulse rate. A sheet of paper pasted to the wall may serve as an excellent work form. As various resuscitative procedures are being carried out, running notes may be jotted on this sheet. This record can be of considerable value later in the course of management.

The medicolegal aspects of any injured patient are becoming increasingly more important. Good records are of considerable value in court. Frequently it is advisable to use color photographs to document the condition of the patient prior to treatment. These photographs should be kept in the physician's files and not released to legal counsel or the court unless the physician is present to interpret them.

Resuscitative Measures.—The physician in charge should designate a competent person to start resuscitative measures as soon as the patient is admitted. Usually a large needle is inserted into an accessible vein and blood drawn for cross matching. This needle is then used for the infusion of a plasma volume expander or an electrolyte solution. When hypovolemia exists, it can be minimized by the use of a plasma volume expander until whole blood is available. It may be necessary for the physician carrying out the resuscitative procedures to perform a tracheostomy or aspirate the chest. After severe injuries, and particularly after injuries about the pelvis, an indwelling catheter should be inserted in the bladder. This will give information as to the presence of hematuria and permit a more accurate record of the urinary output.

In some patients it may be necessary to do a cutdown on an accessible vein and insert a plastic catheter. This provides a good intravenous lifeline. The physician in charge should continue to watch bandaged areas to make sure that hemorrhage is adequately controlled.

In some patients it may be necessary to insert a gastric tube for evacuation of the stomach or as a diagnostic procedure to determine the presence of fresh blood in the stomach.

The patient's general systemic reaction to his wounds and to the resuscitative measures that are being carried out should be carefully observed. If hypotension continues; in spite of adequate fluid and blood replacement, other causes for the hypotensive state should be sought.

Preparation for Definitive Care.—In most instances, the physician in charge should be a general surgeon. He must consider the entire patient. No specialist can avoid being particularly interested in the problems of his own field. As soon as the physician in charge has completed his examination and has started resuscitative measures, he may want to call in consultants representing various specialty disciplines. These consultants should confer with the physician in charge, and a definitive plan of action should be outlined. The management should be defined in such a way that priorities for treatment are properly assigned.

In some hospitals, a roentgenographic diagnosis of a fracture automatically admits the patient to the orthopedic service. A fracture is about the only type of injury that will not kill the patient immediately. In fractures of the pelvis, the bony injury may never be lethal, but a rupture of the bladder or the urethra may result in death if unrecognized for a few hours. Fractures of the lower ribs on the left side frequently are accompanied by a rupture of the spleen or kidney. These are not orthopedic problems. With fractures of the upper ribs, the orthopedic surgeon would be the first to admit that his special training did not include the emergency handling of tension pneumothorax or paradoxical respiration.

Not infrequently, all unconscious patients are admitted to the neurosurgical service. This is an extremely dangerous situation, for the patient cannot communicate concerning pain and tenderness in various areas of the body. The percentage of craniocerebral injuries in which an immediate operation on the skull is indicated is extremely small, but if there is an abdominal injury on the same patient, timing of operation may be lifesaving. Again, the emphasis in care for the patient with multiple injuries is good organization and a physician in charge who keeps all anatomic and physiological areas in mind. After definitive care, certain specific injuries may become the major problem, and the responsibility for the patient can be turned over to whatever specialist is indicated.

Once all of the injuries have been diagnosed, it is necessary to decide which presents the greatest danger to life, which needs treatment first, and which can safely be ignored for the time being. No rule of thumb can be applied to the treatment of multiple injuries except that the lesions which offer the greatest danger to life should be dealt with first.

The restoration of cardiorespiratory physiology must come first, and then treatment of injury to the hollow viscera such as intestines, bladder, and occasionally lung and heart. Treatment of injuries of the liver, spleen, or diaphragm may accompany these procedures, if required. Open injuries of the muscle and bone receive next priority. Usually closed fractures, head injuries, and laceration of soft parts can wait until their care can be tolerated after the aforementioned injuries have been treated. Each treatment should be instituted at the earliest possible moment as decided by the physician in charge.

Definitive Management

As soon as the plan for definitive surgery is made, the patient should be put in the best possible condition for operation. It is most difficult to decide when a patient's blood volume has been increased to the extent that he can best tolerate anesthesia and operation. The value of adequate preparation for operation has frequently been emphasized in elective surgery. In the surgery of the injured man, it is even more important to prepare the patient by restoring his blood volume before operation. Unless continued hemorrhage is present and operation is mandatory to control this hemorrhage, the blood volume should be increased to near-normal levels by transfusion. Frequently, blood requirements may be judged by the size and character of the wound. The surgeon's guide to the adequacy of restorative treatment consists of general appearance of the patient, color of the conjunctiva, blood pressure level, pulse rate, and output of urine. If sufficient blood has been provided to permit good peripheral circulation, it will usually be indicated by the blood pressure. The adequacy of visceral blood flow can be estimated by the rate of urine flow. In the severely wounded patient, the output of 30 cc. or more of urine per hour suggests that the circulatory volume is approaching normal. The patient is usually ready for operation when the systolic blood pressure reaches 100 to 110 mm. Hg and his pulse rate falls to 120 per minute or less. In some instances, hemorrhage may occur as rapidly as blood is being replaced. In such cases, blood should be pumped through two or three veins and the patient should be placed on the operating table immediately. As soon as the hemorrhage is controlled at operation, further manipulation should be deferred until the blood volume deficiency has been restored.

Problems of anesthesia in relation to trauma are usually in direct proportion to the extent of injury. The best possible estimate of the condition of the patient will go far toward enabling the proper choice of anesthesia. The anesthesiologist should be consulted, along with other specialists involved, in the management of the patient and a general decision made with all of the facts at hand concerning the type of anesthesia best suited for the patient and the operative procedure. Occasionally, one may be confronted with an excessively depressed patient as the result of overdose of a narcotic prior to transportation. Nalorphine (Nalline) hydrochloride may be a worthwhile drug to use in such circumstances. It antagonizes the respiratory and circulatory effect of the opiate. The selection of the anesthetic agent is rarely as important as is the person giving the anesthetic. The anesthesiologist should choose the type of anesthetic agent with which he is most familiar and is best suited to the over-all condition of the patient.

The surgeon may, with the help of his assistants, operate on one region of the body after another. In some instances, two surgical teams may operate simultaneously. For example, a patient suffering from an abdominal wound and a craniocerebral injury, accompanied by hemorrhage from the cranial wound, may be operated on first by the neurosurgeons, and then as a second procedure, a laparotomy can be carried out. If hemorrhage is occurring from both areas, two teams might operate simultaneously. It is not infrequent that two surgical teams operate on the abdomen and an extremity at the same time. The general condition of the patient and the further trauma of the operative procedure determine whether or not simultaneous operative procedures are warranted. In critically ill patients, the most-needed procedure is carried out first, and then, if the patient's condition permits, a further operation may be performed as a subsequent procedure.

The use of prophylactic tetanus immunization and early administration of antibiotics should always be considered. Wounds should be cleansed and properly débrided. Much loss of time and possible infection will be alleviated if wounds can be cared for early. On the other hand, soft tissue wounds usually do not endanger life, and their treatment further increases the hypovolemia. Since soft tissue wounds can be handled at any time, it may be necessary to apply a dressing and care for them later. When burns are associated with mechanical injury, the systemic effect of the burn should be corrected early by administration of the appropriate fluids. As soon as the patient is prepared for operation, the mechanical injury can be treated. If fluid loss from the burn is being adequately replaced, the best time for the patient to withstand operative procedures is during the first few hours. After treatment has been given to the accompanying injury, local therapy of the burn wound can be accomplished, but this should receive lower priority.

Emotional stress as well as physical discomfort must be alleviated as much as possible. The physiological stress from the injury is usually a tremendous one, and it is the physician's responsibility to alleviate as much of the emotional stress as possible. If it is feasible, the physician should discuss the injuries with the patient and dispel any uncertainties that might have arisen in the patient's mind. Above all, the physician should pay particular attention to keeping the family appropriately informed. This helps to establish better rapport with the patient, gain his confidence, and is an important facet of the physician's art.

Summary

The patient with multiple injuries frequently receives inadequate treatment, because physicians are poorly informed and there is improper organization for the patient's care. The physician who first sees the patient with multiple injuries has a grave responsibility. He must arrest the continuing effects of the wounds and start restoration of the patient's condition. It is his responsibility to carry out the necessary resuscitative measures to prepare the patient to withstand the further trauma of transportation to the hospital.

In the hospital one physician should take charge. He should direct the over-all resuscitation and preparation for definitive care. Usually it is best if this physician is a general surgeon. He can call in the necessary specialists, but he must make the final decisions and assign priority of management. The secret to good definitive care is adequate preparation for operation. In the initial hospital management, there should be a careful appraisal of all injuries followed by adequate preparation for definitive operative procedures.

TREATMENT OF CANCERS ARISING IN SCARS.—Cancers arising in burn scars, sinus tracts, and fistulae are often locally extensive and destructive but usually do not metastasize. In a few instances local lymphnode metastases and even hematogenous metastases are reported, but these are unusual. These tumors are usually well-differentiated and slow-growing. From the literature, one gains the idea that these cases have a poor prognosis. This hardly seems justified when radical measures are employed to remove the lesions and if they can be diagnosed early. In all probability, we shall see a diminishing number of cases, since burns are almost routinely being skin-grafted and since antibiotics and chemotherapy are so successful in preventing or curing chronic infections. Moreover, such premalignant lesions as old burn scars which are extensive and subject to irritation, chronic osteomyelitis tracts, and fistulae of various sorts should preferably be removed surgically if possible.—R. F. Bowers, M.D., and J. M. Young, M.D., Carcinoma Arising in Scars, Osteomyelitis, and Fistulae, *A.M.A. Archives of Surgery,* April, 1960.

ANTIMICROBIAL THERAPY IN INJURED PATIENTS

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It is a well-established fact that hemorrhage, shock, impairment of respiration, and infection are the complications most dreaded in injured patients.[1] Wounds of violence are particularly prone to develop infection because of their gross contamination, the presence of large areas of devitalized tissue and retained foreign bodies (fig. 1), the involvement of regions particularly susceptible to infection, the frequent association of vascular injuries, and delayed or faulty surgical therapy.[2] The development of infection in wounds increases the period of morbidity, produces further destruction of tissue, suppresses the process of healing, and may have a significant effect on mortality.[3] Tissues destroyed by bacterial invasion are usually replaced by scar tissue which may affect function as well as cosmetic appearance.

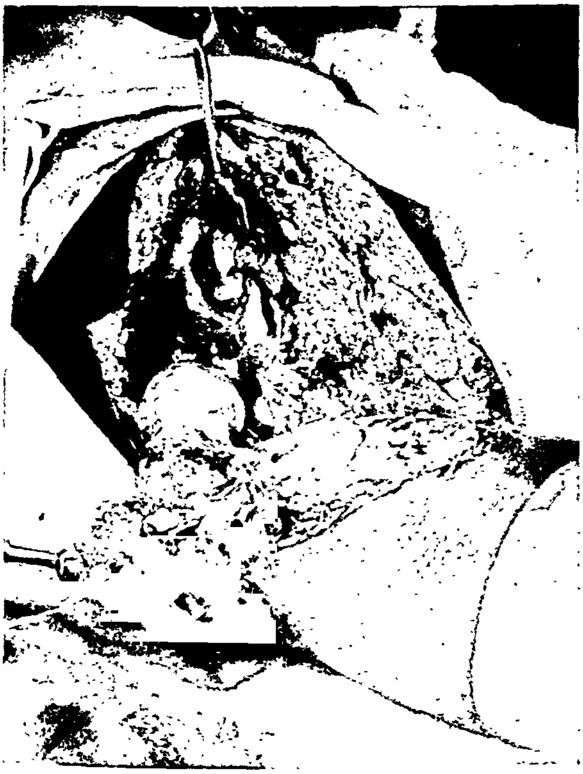

Fig. 1.—Crushing injury of hip resulting from train accident. Note traumatic disarticulation of head of femur, extensive damage of soft tissues, laceration of femoral arteries, and gross contamination, conditions which predispose to development of severe wound infection.

General Considerations

Unfortunately, infection, the greatest enemy of wound healing, continues to be a serious problem, aseptic technique and antibiotic therapy notwithstanding. The primary basis of this form of infection is the successful growth of micro-organisms within the wound itself and their invasion of the physiological interior of the body. Experience has shown that bacteria may be present in a wound without producing clinical evidence of infection and that certain factors influence their growth and invasion. Normal tissues have a remarkable resistance to micro-organisms and their effects, whereas irritated or devitalized tissues have limited or little capacity of resistance.[4] Dead tissue remaining in a wound invites and supports the growth of virulent as well as relatively nonvirulent or saprophytic organisms.

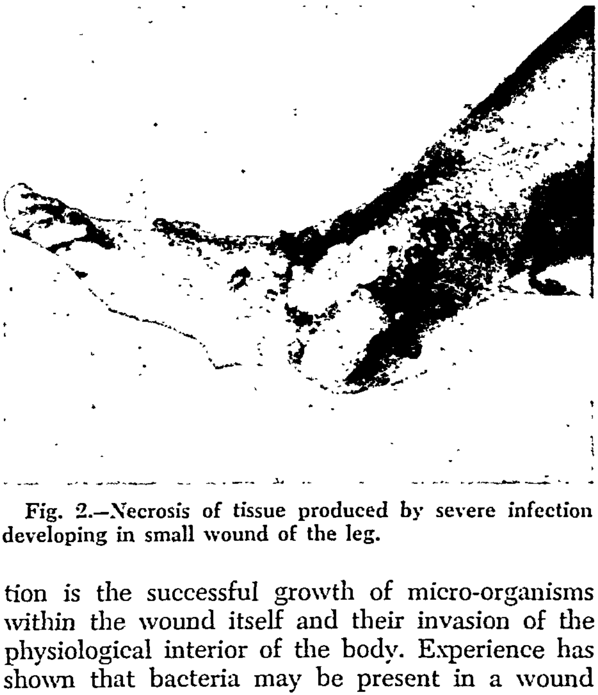

Fig. 2.—Necrosis of tissue produced by severe infection developing in small wound of the leg.

The physical condition of the injured patient may also be an important predisposing factor to infection. General debility, severe dehydration, prolonged shock, malnutrition, exhaustion, metabolic disorders such as uncontrolled diabetes or cirrhosis, marked anemia, steroid therapy, leukemia, or recent and extensive x-ray irradiation may lower his general or local resistance sufficiently to permit bacterial invasion.[5]

Thoughtful consideration of the foregoing facts leads to certain general conclusions. The development of local wound infection depends primarily on the altered physiological state of the wound. If

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devitalized tissue is permitted to remain or develop in the wound, bacterial growth and infection are probable, in the face of the concomitant contamination (fig. 2). It may also be assumed that antibacterial therapy is necessarily adjunctive treatment and of secondary importance to early and adequate operation.[6]

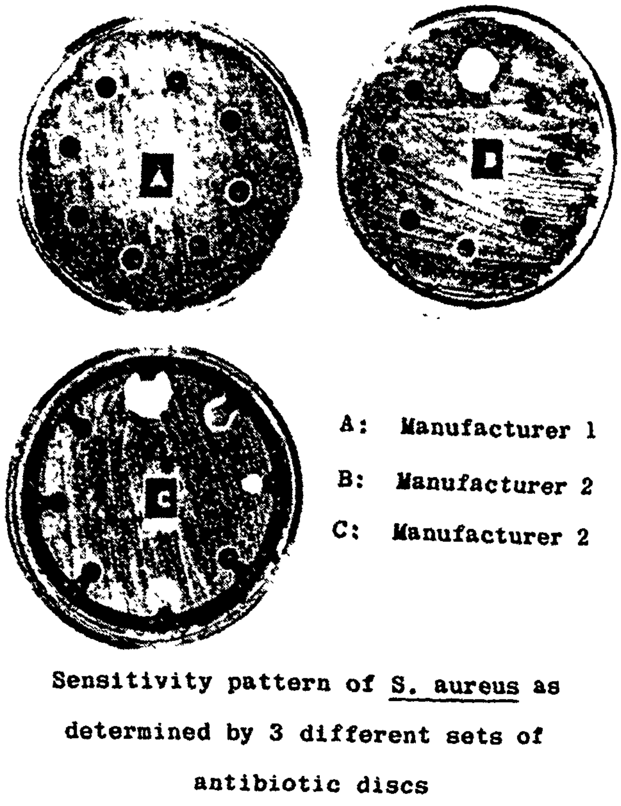
Fig. 3.—Fulminating anaerobic cellulitis of abdominal wall originating from left inguinal wound. Radical incision and drainage were mandatory to arrest rapid spread of infection.

The chief benefit of antimicrobial therapy lies in the attenuation, limitation, or control of infection by residual micro-organisms in the wounds after débridement and operative repair, or in the localization of infection developing within wounds in which surgical treatment is necessarily inadequate, delayed, or impossible. Clinical experience has repeatedly shown that all of the various antibacterial agents must be used intelligently to obtain their full effects. Failure to observe certain established principles in the management of injured patients with antimicrobial agents may result in incomplete or limited effects or even failure. The purpose of this discussion is to review these factors as well as the indications, methods, value, and limitations of practical antibacterial therapy in wounded patients for the prevention or treatment of various infections which may complicate trauma.

Special Considerations

Accurate and Complete Diagnosis.—The importance of a correct clinical diagnosis and evaluation of the injured patient's condition is fundamental. Careful examination should be done to determine the cause, location, nature, extent, and duration of the injuries. The existence of shock and the presence of special wounds such as crushing injuries, or penetrating wounds of the abdomen, chest, or central nervous system should be noted. General factors which might contribute to bacterial invasion such as diabetes mellitus or concomitant steroid therapy should be detected, if present. Additional valuable information can be gained as to the probable types of contaminating or infecting bacteria. Observation may suggest the kind of infection and whether it is localized or invasive, mild, serious, or fulminating. Immediate examination by smear and culture of exudates obtained from infected areas are also recommended for additional diagnostic information.

Proper Timing of Operative Treatment.—If only bacterial contamination exists in wounds, prompt surgical excision and removal of all the devitalized tissue, clotted blood, and foreign bodies within six to eight hours after injury are most important. Antimicrobial therapy should be started before operation, however, and continued postoperatively. If bacterial infection has been established, surgical excision of the infection is generally impossible. Other necessary operative procedures may be delayed to advantage until the invasive qualities of the infection have been overcome by antimicrobial therapy or have been limited by less extensive procedures, such as incision and drainage of abscesses or areas of necrotizing cellulitis, or the removal of sloughing tissue, sequestra, or foreign bodies. In certain infections, such as gas gangrene, anaerobic cellulitis, and acute hemolytic streptococcic gangrene, emergency surgical decompression by radical incision and drainage may be necessary (fig. 3).


A
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A: Manufacturer 1
B: Manufacturer 2
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Sensitivity pattern of S. aureus as determined by 3 different sets of antibiotic discs

Fig. 4.—Variations in sensitivity patterns to penicillin, chloramphenicol, oxytetracycline, and tetracycline for hemolytic Staphylococcus pyogenes var. aureus as determined by commercial disk method.

Selection of Effective Antibacterial Agents.—The selection of the antibiotic agent should be made on the basis of its effect on the contaminating or infecting bacteria presumed or known to be present. When possible, one or two effective agents should be used instead of a "shotgun" mixture of three or more agents. Evidence indicates that the use of multiple agents will not prevent the development of infection by organisms such as the hemolytic Staphylococcus pyogenes var. aureus and the various gram-negative bacilli if the local conditions are favorable. Of more importance is the fact that infection emerging under the screen of multiple antibiotic therapy will be caused by bacteria resistant to the antibiotics used as well as to other related antibiotic agents. Antibiotic sensitivity tests are recommended in the selection of antibiotic agents for the treatment of serious or prolonged infections whenever possible. It is important, however, to keep in mind the possibility of error in results of sensitivity tests done by the commercial disk method (fig. 4).[7]

Adequate Dosage.—The dose of the antibiotic agent chosen should be sufficiently large to produce antibacterial concentrations in the blood, tissues, and exudates at the sites of injury or infection. In addition, the duration of therapy should be sufficiently long to permit the natural defense mechanisms of the body to dispose of the inhibited, but often still virulent, bacteria. Since most agents exert only a bacteriostatic effect, failure to continue treatment long enough may result in the delayed appearance or exacerbation of an infection. Experimental and clinical data also suggest that progressively larger doses of some of the antibiotics, notably penicillin, have an increasingly greater antimicrobial effect (fig. 5).[8]

Method of Administration.—Wounds of violence are frequently associated with shock produced by one or more causes. This complication may affect the method chosen for the administration of antibacterial agents. If shock is present, absorption of antibiotic agents given by intramuscular or oral routes may be retarded, inadequate, or capricious.[9] For this reason the intravenous route is recommended until the shock has been adequately treated and controlled. The local application of chemotherapeutic agents to wounds is seldom indicated in the management of patients with acute injuries and is not recommended.

Early Treatment.—The earlier that antibiotic therapy is started after injury the better its effects. Generally speaking, the antimicrobial agent selected should be administered intravenously promptly after the seriously injured patient is admitted to the hospital and before he is taken to the operating room. If infection has already developed, early therapy gives the best chance of obtaining rapid and prompt control of the invasiveness of the process, with either spontaneous resolution of the lesion or limitation of the bacterial slough to a minimum.[10] Delayed or late treatment usually is less effective, but it often permits localization of the process and indicated surgical procedures when the patient's general condition has been restored to a normal or a near-normal state.

Complications.—A variety of complications or untoward reactions may develop in patients undergoing antibiotic therapy with any of the agents.[11] It is important for the clinician to be informed as to their nature and to be alert for their occurrence. Those complications caused directly by the antimicrobial agents include (1) toxic reactions related to the type and amount of drug given, (2) hypersensitivity reactions, and (3) idiosyncrasies.[12] Although toxicity of the various agents differs considerably, each of the drugs has been shown to be capable of producing one or more types of reaction. Those produced by overdosage can be readily prevented or controlled, but the accumulation of high serum concentrations in aged or debilitated patients can be overlooked easily. Those secondary to hypersensitization of the patient are becoming of increasing importance, particularly in the instance of penicillin. Fortunately, idiosyncrasies to these agents including chloramphenicol (Chloromycetin) are exceedingly rare.

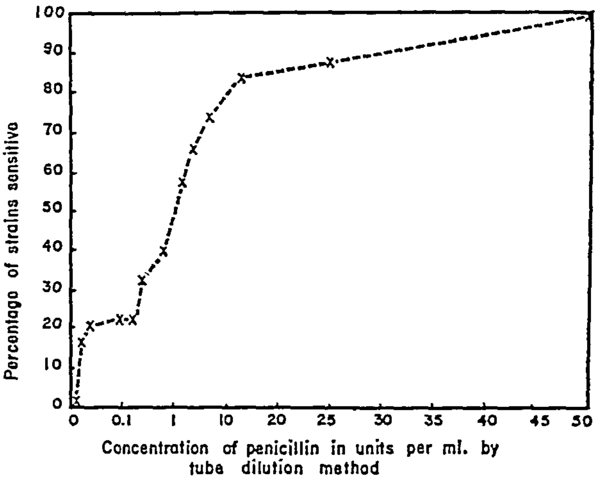

Fig. 5.—Curve indicating increasing percentage of susceptibility of 48 strains of hemolytic Staphylococcus pyogenes var. aureus to progressive concentrations of penicillin, with 85% being sensitive to 12.5 units of penicillin per cubic centimeter (ml.).

Another complication of increasing importance is the secondary or superinfection caused by antibiotic-resistant bacteria. The suppression of sensitive bacteria in mixed infections by antibiotics may be followed by a marked change of the bacterial flora in the wound or in the systemic tracts. Under these circumstances bacteria which are normally of lesser virulence may become invasive and may even invade the blood stream. Such infections have generally been produced by the hemolytic Staph. pyogenes var. aureus and gram-negative bacilli such as Proteus vulgaris, Pseudomonas aeruginosa, Escherichia coli, and Aerobacter aerogenes.

Another complication which may occur in the seriously injured patient is the masking of infection which develops in the vicinity of the wound or elsewhere in the body. This masking makes the recognition and localization of the infection difficult.

Supportive Therapy.—In recent years the importance of adequate supportive treatment in injured patients undergoing antibiotic therapy has been emphasized. The full therapeutic effect of the antibacterial agent will not be obtained if serious derangements in local and general physiology are overlooked or uncorrected. More recent evidence indicates that the effectiveness of certain antimicrobial drugs, particularly chloramphenicol, can be significantly enhanced by the concomitant use of pooled immune serum globulin in case of overwhelming or serious long-standing infections.

Prophylaxis in Acute Trauma

Prophylactic antibacterial therapy is recommended promptly for all patients with serious wounds of violence such as major open soft tissue wounds, compound fractures, penetrating wounds of the abdomen, the chest, or both, penetrating wounds of the central nervous system, injuries involving the oral or pharyngeal cavities, and injuries of the perineum. The antimicrobial therapy should be given systemically as soon after injury as possible and continued postoperatively. If the patient is in shock, the chemotherapeutic agent should be administered intravenously for reasons described previously.

Soft Tissue Wounds and Burns.—No antibiotic therapy is recommended for trivial or minor injuries. The following agents are recommended for initial prophylaxis in serious or severe injuries: 1. Aqueous sodium penicillin G or potassium penicillin G (Dramcillin, Dropcillin, Penalev, Pentids, Potassium Penicillin G), 250,000 to 500,000 units, may be given intramuscularly or intravenously every six to eight hours for five days in patients who are not sensitive. Erythromycin (Ilotycin) ethyl carbonate or erythromycin (Erythrocin) lactobionate may be used as an alternate. It is questionable whether any significant additional protection can be obtained from the combined use of penicillin with a broad-spectrum antibiotic. Accumulative data indicate that invasive infections by beta-hemolytic streptococcus and pneumococcus can be successfully prevented by antibiotic prophylaxis, but there is little or no similar evidence of successful prevention of infections by the hemolytic Staph. pyogenes var. aureus, Ps. aeruginosa, P. vulgaris, Esch. coli, and other gram-negative bacilli. 2. If desired, one of the broad-spectrum antibiotics such as chloramphenicol, demethylchlortetracycline (Declomycin), tetracycline (Achromycin, Panmycin, Polycycline, Steclin, Tetracyn) hydrochloride, chlortetracycline (Aureomycin) hydrochloride or oxytetracycline (Terramycin) hydrochloride may be given systemically in doses of 500 mg. every eight hours, or 250 mg. every four hours, and continued for three or four days. The need for such therapy is then reconsidered and continued, discontinued, or modified as indicated by the presence or absence of infection. 3. For patients with less severe wounds, the oral route may be used to advantage for the administration of either penicillin or the broad-spectrum agents.

Compound Fractures.—The same general plan of prophylaxis as outlined in the preceding paragraph is generally useful. In patients with wounds exhibiting extensive tissue necrosis along with compound fractures, larger doses of penicillin, up to 1,000,000 units of an aqueous soluble salt of penicillin G every three hours, may be indicated.

Penetrating Wounds of Abdomen.—There is considerable evidence that antimicrobial therapy is of great prophylactic value in preventing death from peritonitis and sepsis in patients with penetrating wounds of the abdomen. Adequate systemic antimicrobial therapy used in conjunction with early surgery has reduced the mortality in such patients from 40 to 60% to 9 to 11% and has minimized peritonitis as a cause of death. It is recommended that the antimicrobial therapy be given preoperatively, intravenously, and as soon after the patient's admission to the hospital as possible in an effort to inhibit bacterial growth intraperitoneally and to provide an antibacterial concentration in the peritoneal fluid at the time of operation.[13]

The following plan has been used at the Cincinnati General Hospital during the past 10 years: 1. One million units of an aqueous soluble salt of penicillin G in sodium chloride injection or 5% dextrose in water for injection is administered intravenously as soon after the patient's admission to the receiving ward as possible and as part of his preoperative resuscitation therapy. 2. At operation, no antimicrobial agents are instilled into the peritoneal cavity. 3. Postoperatively, 500 mg. of one of the tetracyclines or chloramphenicol is administered intravenously along with penicillin. 4. An aqueous soluble salt of penicillin G in doses of 250,000 to 500,000 units is recommended every six hours intramuscularly for five days.

One of the tetracyclines or chloramphenicol in doses of 500 mg. is given intravenously every 12 hours for four to six days. At the end of this period, antibiotic therapy is discontinued if there is no obvious infection, continued until the infection has been controlled, or modified as indicated by the emergent antibiotic-resistant infection.

Penetrating Wounds of Chest.—A plan of antibacterial prophylaxis similar to that described in the section on penetrating wounds of the abdomen may be used.

Therapy of Established Infections in Acute Trauma

Therapeutic antimicrobial therapy is of considerable value in the control of established infections developing in the injured patient when started early and based on the various factors or principles discussed previously under special considerations.

Local Infection.—For patients with slight or moderate local infection in whom no serious infection is anticipated, the same antimicrobial dosage schedule is recommended as that described for prophylactic use in soft tissue wounds. This plan should be modified on the basis of any demonstrated antibiotic resistance of the bacterial infections which emerge under the prophylactic antimicrobial treatment.

Invasive Staphylococcic and Streptococcic Infections.—In injuries with established invasive infections localized to the tissue surrounding the wound, or the regional lymphatics and lymph nodes, antibiotic therapy should depend on the infecting bacteria. In hemolytic streptococcic or staphylococcic infections of moderate severity or regional invasiveness, the choice of the antibiotic treatment may be made from the following agents: (1) an aqueous soluble salt of penicillin G, 100,000 to 500,000 units every four to six hours intramuscularly in the absence of patient sensitivity to penicillin; (2) for penicillin-resistant staphylococcic infections, chloramphenicol, demethylchlortetracycline, tetracycline, oxytetracycline, chlortetracycline, or erythromycin in doses of 250 mg. orally every four hours, depending on the demonstrated sensitivity results; (3) an aqueous soluble salt of penicillin G in large doses of 1,000,000 units every three or four hours (fig. 5); (4) vancomycin (Vancocin) hydrochloride administered parenterally in doses of 250 mg. every six hours; this agent is still in short supply and relatively expensive, however; and (5) continuation of adopted therapy until infection is under control and fever and white blood cell counts are normal for five to seven or more days.

In systemically invasive or fulminating streptococcic and staphylococcic infections, the same plan may be adopted, with consideration of increasing the dosage, shortening the interval between doses, and administering by the preferential intravenous route.

Mixed Bacterial Infections.—In severe infections caused by fecal bacteria, such as peritonitis, retroperitoneal cellulitis, crepitant cellulitis, putrid empyema, and mixed infections of the buttocks, thigh, or perineum, essentially the same antimicrobial agents may be used as in prophylaxis of penetrating wounds of the abdomen, plans 1, 2, and 3. The broad-spectrum antibiotic should be selected on the basis of demonstrated sensitivity of the infecting bacteria and should be given in larger doses of 500 mg. every four to six hours. Chloramphenicol has been particularly effective in our experience when used with penicillin and immune serum globulin given intramuscularly. The importance of recognizing and draining intraperitoneal or retroperitoneal abscesses masked by antibiotic therapy cannot be overemphasized.

Clostridial Infections.—In established clostridial myositis or true gas gangrene, the choice of effective antibiotic therapy may be made from the following regimens: 1. Chlortetracycline, oxytetracycline, tetracycline, or chloramphenicol may be given intravenously in doses of 500 mg. every six to eight hours. Both experimentally and clinically, however, the tetracyclines have been the drugs of choice in this serious infection.[14] 2. An aqueous soluble salt of penicillin G in doses of 1,000,000 units given intramuscularly every three hours may also be effective. As seen in figure 6, it has been shown experimentally that increasingly large doses of penicillin G have a progressive effect in controlling experimental clostridial infections and in decreasing the incidence of death.

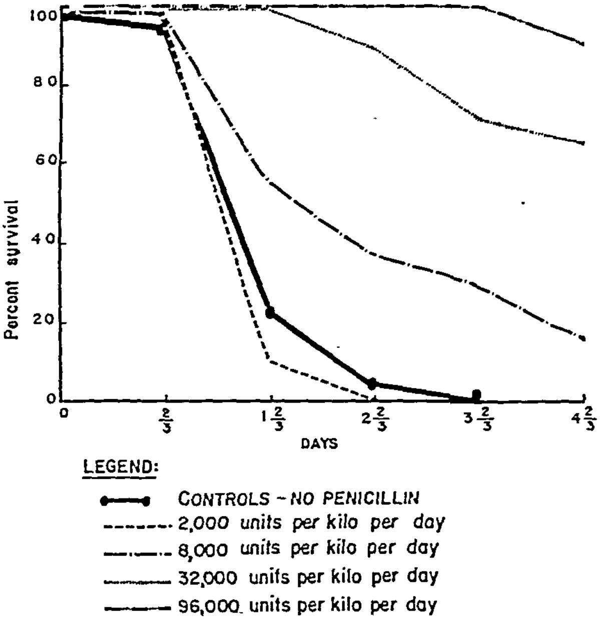

Fig. 6.—Effect of immediate penicillin therapy on experimental gas gangrene.

For patients with clostridial cellulitis, the same two plans of antimicrobial treatment are used at the Cincinnati General Hospital.

Tetanus.—There is no scientific evidence to indicate that antibiotics have any effect on circulating tetanus toxin or toxin fixed in the central nervous system. There is also lack of evidence to indicate that antibiotic therapy can affect mortality except through the control of secondary infection, such as pneumonitis or associated bacterial infections of the wound. It is usually agreed that patients with tetanus should be given antibiotic therapy in an effort to prevent or control the pneumonitis which frequently occurs as a result of the prolonged sedation, aspiration of the increased volume of secretions during convulsions, or impairment of respiration.

Serious Pseudomonas (Pseudomonas aeruginosa) Infections.—These infections may be treated with the following antibiotics: 1. Polymyxin B (Aerosporin) sulfate, 2.5 mg. per kilogram of body weight, may be given in 24 hours, the amount being divided into three or four doses which are administered under close observation every six or eight hours for a period of five to seven days. Pain at the site of intramuscular injection may be appreciable, but it can be reduced by the addition of a 1% procaine solution as a diluent. Because of the toxicity of polymyxin B sulfate, a daily dose of 200 mg. should not be exceeded, and patients undergoing therapy should be observed closely for signs of renal or neurological toxicity. Few, if any, strains of Pseudomonas are resistant to polymyxin B sulfate in concentrations of 12.5 mcg. per cubic centimeter. 2. Chloramphenicol, tetracycline, oxytetracycline, chlortetracycline, or demethylchlortetracycline may be used, but they are generally less effective.

Septic Shock.—Occasionally, patients with injuries will develop a state of clinical shock not attributable to the usual causes, such as hemorrhage or trauma. This condition, when associated with proved serious infection, may be septic shock which characteristically occurs two to five days after injury. In studies at the Cincinnati General Hospital,[15] it is interesting to note that acute diffuse peritonitis accounted for 54% of the cases of septic shock and that large intra-abdominal abscesses with peritonitis were responsible for an additional 12%. Extensive soft tissue infection of the abdominal wall or perineum was another important cause.

On the basis of our experimental work, the following plan of treatment has been evolved and used at the Cincinnati General Hospital during the past three years and is instituted as soon as a diagnosis of septic shock has been made: 1. Fluids are immediately infused by the intravenous route, particularly normal human plasma or blood, in an attempt to correct any deficiency of the circulating blood volume without overloading the circulation and producing pulmonary edema. 2. Massive doses of antibiotics are administered by the intravenous route. The agents chosen for each case vary, and, in the absence of specific sensitivity data, the selection of the antimicrobial agent necessarily must be made on an empirical basis. Antibiotic-sensitivity data, when available, are helpful for specific selection of the antimicrobial agent. The existence of shock makes the intravenous route advisable and particularly important, not only because of the impairment of absorption from other routes but also because of the urgent need for a rapid chemotherapeutic effect. 3. Levarterenol (Levophed) bitartrate administered intravenously by drip, in a solution of 5% dextrose and water for injection, may be used to restore the blood pressure to a level of 80 mm. Hg or above. This is done in an effort to maintain the various physiological functions, particularly renal, until the infection is brought under control. 4. Oxygen is administered continuously by nasal catheter or tent. 5. The foot of the bed is elevated 12 to 18 inches. 6. An indwelling catheter should be used to measure the hourly urinary output, which is maintained between 25 and 75 cc. per hour by the regulated administration of fluids and levarterenol. 7. Cortisone (Cortisone, Cortogen, Cortone) acetate or hydrocortisone (Cortef, Cortril, Hycortole, Hydrocortone) is probably not indicated unless a blood pressue of 90 mm. Hg or more cannot be restored by the administration of fluids and levarterenol. Under these circumstances, it has been our experience that hydrocortisone has been useful in extending the patient's life until the severe infection could be controlled by intensive antibiotic therapy and any indicated surgical treatment. 8. Timed surgical intervention is recommended, when indicated and feasible.

Previous to the adoption of this therapeutic regimen, the occurrence of circulatory failure in a patient with a severe infection was usually followed by death within a matter of hours. Since its adoption, 36% of the patients with septic shock have been treated successfully at the Cincinnati General Hospital.

Summary

Infection continues to be a major problem in the treatment of patients with wounds of violence. Prophylactic antibacterial therapy has failed to decrease significantly the incidence of infection as a complication of injury, except in the instances of those produced by beta-hemolytic streptococcus and pneumococcus and in penetrating wounds of the abdomen and chest. Nevertheless, prophylactic antimicrobial treatment is recommended, since there are data to indicate that many infections developing within wounds are localized or attenuated by these agents.

On the other hand, antimicrobial treatment has been of considerable value in the control of established infections which complicate wounds, provided use of these agents has been adjunctive to surgical treatment and has been based on certain proved principles which have been discussed.

As a consequence of the misuse of these antibacterial agents, a number of problems have been created, one of which has been an increased incidence of emergent antibiotic-resistant bacterial infections. Such lesions are doubly serious and more difficult to control. It is recommended that more

thoughtful and conservative use of antibiotics be adopted in the management of patients with injuries, in an effort to avoid the allergic reactions, secondary or superimposed infections, emergent-resistant infections, and antibiotic toxicity from excessive doses of the broad-spectrum antibiotics. Clinical experience indicates that wound infections are, and will continue to be, a serious problem as long as their prevention and control are dependent primarily on the prophylactic use of antimicrobial agents and not on early and adequate surgery in association with their adjunctive use.

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THE ROLE OF GLUTEN IN IDIOPATHIC CELIAC DISEASE.—Celiac disease is thought to be a basic constitutional defect. . . . Gluten does not cause the symptoms, but may be one of the trigger mechanisms. Not every patient with normal pancreatic function and chronic steatorrhea responds to a low gluten diet in which wheat, rye, oats, and barley are omitted. . . . Some respond to a diet containing selected wheat products, i. e., melba toast, zwieback, angel food, or sponge cakes, if used in limited amounts. However, they do not tolerate other wheat, rye, oat, or barley foods, . . . until they are near adolescence or beyond. . . . The fat tolerance in celiac disease is in direct proportion to the tolerance of gluten. The more highly unsaturated fats (corn, cottonseed, soybean, sesame, and olive oils) are used in limited amounts in the early stage of the mild phase. Their quantity is gradually increased with improved appetite and clinical status. Following this, the polysaturated fats may be introduced. Hard fats of meat and bacon are usually poorly tolerated, as are foods prepared with excess fat. It is important to include a suggested meal plan when giving instructions to patients. Frequently parents cannot formulate such a plan when given only a list of foods to allow and avoid. Also, parents should be alerted to read labels on all prepared foods carefully. . . .—E. M. Mike, B.S., Practical Dietary Management of Patients with the Celiac Syndrome, *The American Journal of Clinical Nutrition,* July-August, 1959.

J.A.M.A., June 4, 1960

CONTROL OF SUFFERING IN SEVERE TRAUMA

USEFULNESS OF A QUANTITATIVE APPROACH

Henry K. Beecher, M.D., Boston

I have chosen the word "suffering" instead of "pain" because it more accurately describes the problems to be considered here. In recent years it has been found possible and rewarding to deal with subjective responses—symptoms—in a quantitative manner. There is no time now to describe the technical approaches to these problems. In any case, such descriptions are readily available.[1]

The problem of pain is doubtless as ancient as the human race, and, perhaps because it is so old, it seems to have gathered about it more folklore than anything else in medicine. In the present instance, the quantitative approach has made it possible to recognize and dispose of some unfounded traditional statements. This might be called a negative benefit. There are positive ones as well. The necessary validation for the statements to be made can be found in the references already given. It might be well to mention for those who are not familiar with the work of recent years in this field that one can, so to speak, titrate the pain of postoperative wounds of a group with two series of solutions, each series containing different but unknown concentrations of morphine, and, using the approved double-blind technique, find, when the codes are broken, that one has equilibrated 10 mg. of morphine to 10.8 mg., an 8% error. Sound mathematical usage requires that regression lines be calculated for the two curves involved, which adds 2% more, so one can work with a total error of 10%.[2] That is, I submit, about as accurately as one can make objective measurements, such as blood pressure determinations and red blood cell counts, in man.

Reaction Factor

One of the positive benefits of the quantitative approach has been the emergence of factual support for a 65-year-old hypothesis. In 1894, Marshall[3] prepared the way for a crucial assumption first grasped by Strong[4] in 1895. In effect, Strong said that suffering has two major components: First, there is the original sensation, produced, in the case of pain, by stimulation of pain endings by some noxious agent. Second, there is the meaning of this sensation, called the reaction or processing component.[5] Strong must be credited with an important working assumption. As far as one can tell now, this was one of those intuitive, almost clairvoyant, insights, for Strong had no clear factual data to support his assumption. Strong factual support has been obtained for it.[6]

Since the factual supporting data are highly pertinent to our discussion, it will be well to summarize these facts. The assumption can be restated to advantage: The significance of the wound determines the suffering therefrom. Evidence for the existence and importance of the reaction component can be seen in the extraordinary effectiveness of placebos.[7]

Thirty-three per cent of persons with severe pain of pathological origin are satisfactorily relieved by placebos. (What constitutes satisfactory relief is, of course, carefully defined and standardized.)

Only 3% of persons with pain as ordinarily contrived experimentally have such pain relieved by placebos.[8] Thus, placebos seem to be more effective when the stress is great than when it is less.

Even large doses of morphine will not dependably alter the experimental pain threshold as usually produced,[1a] yet a small dose of morphine will completely relieve the pain of a great wound.

Of men severely wounded in battle, but mentally clear, who were not in shock and who had not received morphine or other analgesic at all in many cases and in no case within four hours, only 25% stated, in response to a direct question, that they had enough pain to want anything done about it.[9] Yet civilians with far smaller postoperative wounds have sufficient pain in over 80% of the cases to require medication for it.[10] This is true whether the operation has been for a long-wasting disease, as cup arthroplasty of the hip for degenerative arthritis, or whether it has been performed for the treatment of a fresh fracture. These two groups compared present strong evidence that the significance of the wound determines the suffering therefrom. The soldiers mentioned were chiefly on the Anzio beachhead where the shelling never stopped day or night for months. The war was suddenly over for the person who was wounded. The wound was a ticket to the relative safety of the hospital and a ticket home. The wound was construed as a good thing. With civilians, however, the necessity for surgery is usually considered to be a disaster. It does indeed appear that the significance of the wound—the reaction component—was the crucial factor in the suffering experienced.

I well remember a rainy night on the Anzio beachhead. The blackout canvas of the shock tent was suddenly thrust aside, and three litter bearers carried in a wounded soldier who was screaming to get off the litter. He thought he was lying on his rifle. It was impossible to examine him in his wild state. A modest dose, 120 mg., of amobarbital (Amytal) sodium was given intravenously, after

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which the patient became quiet and relaxed. He slept but could be easily aroused. He was not anesthetized. It then became possible to undress and examine him. The "rifle" he had been lying on was, in fact, sensation from eight ribs cut in two by a shell fragment. One rib had punctured the diaphragm and a kidney. This striking example was seen by many physicians. The effectiveness of a relatively small dose of barbiturate in handling the pain of some of the severely wounded was subsequently widely confirmed. It is probable that barbiturates are most effective when injuries are associated with great fear and anxiety. Whether this explanation is correct is beside the immediate point: The foregoing types of information are evidence for the existence and importance of the reaction component. Indeed, it would be next to impossible to explain these observations on any other basis. It is perhaps not too strong a statement to say that they prove the existence and importance of the reaction factor.

Shock and Suffering

It is, of course, not possible to deal very long with severe trauma without encountering the problem of wound shock. In this connection I should like to make several points.

Overusage of Analgesic Agents.—In the minds of too many physicians, the presence of a severe injury or burn is all the indication needed for the injection of a large dose of morphine or other analgesic agent. This may not only be unnecessary but can be, in fact, a dangerous error. Let us consider several common situations. First, as I have indicated previously, there is no direct relationship between the extent of the wound and the suffering experienced from it. (You will recall that 75% of the men wounded in battle and not in shock had no pain or so little they did not want anything done about it, whereas civilians with the comparatively small wounds of surgery required pain relief more than three times as often.) Second, it is curious that so many physicians have overlooked the fact that wounded soldiers in shock rarely complain of pain. I suppose this has been overlooked owing to the almost universal compulsion to give a large dose of morphine first to a wounded man and ask questions later. This procedure results from failure to understand that there is no direct relationship of extent of wound and suffering experienced.

There are three principal reasons why this wrong assumption may be dangerous to the point of folly. 1. The man in shock has probably lost much blood; such patients are exquisitely sensitive to the depressant effects of morphine. 2. The man in shock may have a pneumothorax, and even small doses of morphine can kill and have killed such men. 3. The peripheral circulation is hardly active in shock, so that absorption from subcutaneous or intramuscular deposits will occur exceedingly slowly or not at all.[11] In case the patient is one of the rather unusual ones who truly have pain, no pain relief will occur, and a second or even a third dose may be given, with the consequence that, when the man is resuscitated and warmed up, with restoration of his peripheral circulation, all of the several deposits of morphine will be absorbed at once, and profound morphine poisoning, even death, can occur.[12] This is called delayed morphine poisoning and is inexcusable. If the man in shock truly has pain, one-third of the usual dose of morphine should be administered intravenously. Delayed absorption doubtless lies back of the tradition of giving large doses of morphine to those with extensive burns, chilled as such persons are by the fireman's hose and sometimes in shock. It can easily be seen why the unsound practice of giving large doses of morphine to the burned has grown up, since the morphine is unlikely to be effective unless given intravenously. 4. Less important than the aforementioned points, but still worth taking into account, is the fact that morphine can change a positive fluid balance of the wounded into a negative one through increased sweating and the induction of vomiting, with fluid loss.

Thirst.—As indicated previously, wound pain in the man in shock may not be present. There is, however, a common cause of great suffering in the person in shock, and this is thirst. It is remarkable how neglected this important symptom often is. Even in warfare severe dehydration is rather uncommon in the newly wounded, and it is not present in civilians as a rule; therefore, complaints of thirst are an ominous warning of deteriorating condition. It appears to be directly related to a sharply decreasing circulating blood volume. It is doubtful if mouth washes have any alleviating effect. The treatment is restoration of blood volume.

Mechanical Factors.—The pain of the wounded can often be relieved by improved splinting of the wound. Fractures of the leg result in great distal swelling. The slitting of a tight shoe will release the swollen foot and often lessen, sometimes relieve, the pain of a fractured femur.

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EARLY MANAGEMENT OF FRACTURES

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The early management of fractures embraces both the temporary emergency management and the early definitive management of both open and closed fractures. The temporary emergency management is nothing more than the emergency splinting for transportation to and within the hospital. This is a facet of management of fractures lacking in color, appeal, and, all too often, professional interest. However, it remains an exceedingly important, albeit a frequently neglected, part of early management. Fractures of long bones, particularly those of the lower extremities, must be splinted at the first opportunity if the best interests of the patient are to be served.

Emergency Splinting

The significance of effective emergency splinting must not be underevaluated. It prevents further damage to soft parts by sharp fragments. In so doing, it may prevent the catastrophe of laceration of a major blood vessel or a peripheral nerve or compounding of a closed fracture. It minimizes pain, contributes to resuscitation from shock or helps to prevent it, and makes the casualty transportable with increased safety. Indeed, the ultimate results of the most expert definitive management may be wholly or in part predetermined by the quality of emergency medical care rendered at the scene of the accident.

Emergency splinting for transportation is preferably applied at the scene of the accident by well-trained ambulance personnel or law-enforcement personnel. When a patient with a broken extremity arrives without a splint at an emergency room, however, the obligation of the physician to provide effective splinting immediately, before the patient is transported to the x-ray room or to his bed, is increased rather than diminished. Emergency splinting should be provided by the first person in attendance having the capability, whether professional or subprofessional.

If emergency splinting were a difficult procedure, its omission might occasionally be excused. It is, however, a simple, easy procedure. Emergency splinting for fractures of the long bones of the upper extremity is particularly easy. Almost any kind of short board splint or even a magazine wrapped around the part will provide adequate splinting for fractures of the forearm. Fractures of the arm, including the shoulder, require only the support of the forearm in a sling and the bandaging of the entire extremity to the chest wall. Patients with fractures of the long bones of the upper extremity are usually more comfortable when they are transported in the sitting rather than the recumbent position.

Emergency splinting of fractures of the long bones of the lower extremity is a little more difficult and requires more material, but it remains a relatively easy procedure. For fractures of the femoral shaft, fixed-traction splinting in a Thomas or half-ring leg splint, with a traction hitch being used about the ankle, remains the preferable method. Coaptation splinting with padded long boards, however, is also a highly effective method that is most acceptable. Such material can usually be obtained with little effort. For fractures of the femoral shaft, a long board should extend from the chest wall down the outer side of the extremity. Other short boards are placed along the medial and posterior surfaces of the injured extremity. All boards are bandaged firmly to the extremity, and the long board is also bandaged to the trunk.

For fractures of the bones of the leg, coaptation splinting, with board splints or other comparable material, as previously described, is preferable to fixed-traction splinting. Of course, the lateral board need extend only to the upper thigh. A pillow bandaged firmly about the leg, with or without lateral boards, will provide effective transportation splinting.

In open fractures, only a sterile or clean dressing of the wound is indicated. Protruding fragments should not be pulled back beneath the skin but, rather, should be covered with a dressing and left protruding until the patient reaches facilities for surgery.

Definitive Management

The first step in the definitive management of both open and closed fractures is a choice of method of management by the treating physician. The

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methods of management of fractures may be classified as (1) closed reduction, if necessary, and immobilization; (2) continuous traction, usually skeletal; (3) open reduction, usually with internal fixation; (4) external skeletal fixation, which includes multiple pins incorporated in a plaster cast; and (5) no immobilization or, at the most, only a bandage and sling. Each of the many varieties of treatment for fractures will fall within this classification. The physician must select and institute promptly the method likely to lead to the optimal result under the circumstances in that particular patient. The choice of method necessarily will depend, in part, on the skill and experience of the surgeon and the facilities and equipment available to him. He must make certain that the method selected is effective and adequate, otherwise it must be abandoned in favor of another. Possibly the most common error in the treatment of fractures is to blindly and stubbornly adhere to the method first selected (even though it is not effective) rather than to recognize that another method must be instituted.

Most fractures are best managed by one, and only one, of the five methods just described. Whereas most are best handled by method 1 (closed reduction and a cast), with many fractures it would be doomed to failure. Some fractures should be recognized immediately as requiring the use of method 2 (continuous traction); a great many others, method 3 (the open-operative method); an occasional one, method 4 (multiple-pin fixation in plaster); and in a fair number, method 5 (the no-immobilization method).

As examples, closed reduction in a plaster cast is indicated in practically every undisplaced fracture, most displaced fractures about the wrist, some displaced fractures about the ankle, all fractures of the shaft of long bones in children, except those in the femur, and stable fractures of the tibial shaft in adults. A stable fracture of the tibial shaft is one with a contour usually transverse or near-transverse, which, after reduction, will not slip or override while in a plaster cast. Continuous traction is indicated in most fractures of the femoral shaft in children and in those fractures in adults too comminuted for intramedullary fixation, for some supracondylar fractures of the humerus in children as either Dunlop's skin traction or skeletal traction through the olecranon, and, in the form of a hanging cast, for most fractures of the shaft of the humerus. The open-operative method is immediately indicated for fractures of the neck and trochanteric region of the femur, for fractures of the shaft of the femur if not too comminuted for intramedullary nailing, for separated fractures of the patella and the olecranon, for most unstable fractures of the tibia, for many fracture-dislocations of the ankle, and for selected fractures about the elbow in both adults and children. Occasionally, multiple-pin fixation in a plaster cast will be advantageous for comminuted fractures of both bones of the leg. No immobilization and early active use are indicated in impacted fractures of the surgical neck of the humerus, many undisplaced fractures of metatarsals, and many fractures of the distal phalanges of the fingers.

The timing for the application of each of these methods of management may be exceedingly important. Closed reduction should be carried out as soon after injury as possible. The closed reduction of fractures is more likely to be successful if it is carried out while the hematoma is still liquid and before excessive swelling has developed. The bone fragments may be more easily palpated and manipulated and the plaster cast applied before excessive swelling takes place. By contrast, if efforts at closed reduction are delayed, the soft parts surrounding the fracture become infiltrated with the products of inflammation and are made inelastic and waterlogged, so that closed reduction becomes increasingly difficult.

The closed reduction of displaced fractures should be considered an emergency except in those situations in which general anesthesia is necessary but is contraindicated at the time. Such a situation can easily present itself when the patient is known to have a full stomach. Preferably, a general anesthetic is not administered to a patient who has eaten during the previous eight hours. For practical purposes, a general anesthetic should never be administered to a child for the closed reduction of a fracture unless the child's stomach is known to be empty because the hazard of aspiration of vomitus, with its dire consequences, is too great. In some instances, such as in a displaced supracondylar fracture of the humerus in a child, when the presence of a full stomach precludes administration of general anesthesia, the fracture may require continuous traction, perhaps in the form of Dunlop's traction, to be selected as the desirable method of management in preference to closed reduction and immobilization.

The institution of the other methods of management is not so urgent, but the sooner the fracture is reduced the better for the fracture and the patient. The sooner continuous traction is initiated, the better the chances for reduction. Open reduction is often performed as an emergency, before excessive swelling takes place. For example, in fractures about joints such as fracture-dislocations of the ankle, prompt open reduction as an emergency is usually advisable, barring contraindications. To delay operation in this injury only permits increased swelling, which, in itself, can further delay the surgery beyond the time when the operation may be carried out with the anticipation of the optimal result. When incisions are made through badly swollen tissue, ischemia and necrosis of sutured wound margins may follow. In fractures of the hip in aged patients, the best interests of the patient may be served by prompt operative fixation of the fractures. The severe, immobilizing pain of the fracture will be relieved; the patient may be turned in bed and gotten into a chair promptly, thereby minimizing the danger of pulmonary complications and decubitus ulcers. As a general rule, fractures should be reduced as promptly as possible by whatever method the physician considers is indicated, unless there are concurrent injuries or diseases which demand that definitive reduction of the fracture be postponed.

Early and prompt institution of the indicated method of management is advisable and often mandatory for the best treatment of a fracture. Delays which are avoidable only complicate the problem and predispose to complications and inferior results.

Open Fractures

Open fractures demand prompt definitive management as surgical emergencies. They deserve investigation, appraisal, and treatment in a fully equipped operating room. General anesthesia is indicated, with few exceptions. Stomach lavage to remove gastric contents may be advisable to permit administration of general anesthesia, with less risk of vomiting and aspiration and their dire consequences. The fractured part should be surgically cleaned, prepared, and draped and the wound examined thoroughly. The indicated surgical procedure is determined by the amount of damaged tissue probably remaining in the wound and the degree of contamination.

Hard and fast rules as to the extent of wound surgery in open fractures cannot be made. The situation varies with the magnitude and type of wound. The objectives of surgery in every wound, however, are the same: (1) to make it as free as possible of those things which predispose to infection—that is, dirt, debris, dead and devitalized tissue, and massive blood clot; (2) to determine whether the wound should remain open or be sutured; and (3) to determine how the fracture should be managed.

In the technique of wound débridement, exposure of the depths of the wound must be adequate. As a rule, the wound must be extended. The incision through skin and fascia must be of adequate length to give free access to devitalized muscle, since its excision is a major objective of wound débridement. Healthy muscle is not discolored, bleeds freely, and contracts when pinched; muscle which does not meet these requirements should be excised. Foreign bodies and all dirt and debris should be removed. For thorough irrigation of the wound, saline solution is a valuable cleansing agent. Bleeding vessels should be ligated. Small fragments of bone completely devoid of soft tissue attachment should be removed, but bone which has some muscular or fascial attachment should be left in place as it is usually viable.

After débridement of the wound has been completed (and, perhaps, the fracture reduced), a decision must be made whether to close the wound or to leave it open. When surgery has been performed within the first six hours after injury, when cleansing and débridement have been thorough, and when closure appears to be surgically feasible without excessive tension, closure of the wound by suture is usually indicated. On the other hand, if the surgeon cannot be reasonably certain that the wound has been rid of the pabulum of sepsis or if closure by suture would produce excessive tension on the sutured margins of the wound, either immeiately or after postoperative swelling has taken place, then, an open wound is preferable. The error should be made on the side of leaving the wound open because delayed closure may be carried out with increased safety several days later. It seems reasonable to state that too many primary closures over open fractures are attempted, and the advantages of an open wound, with delayed closure, are too often overlooked.

Insofar as the fracture is concerned, the same methods of management, in general, are applicable to open or closed fractures. In the former, however, the question of using internal fixation at the time of wound débridement often arises. Internal fixation of open fractures is a calculated risk which requires expert judgment, but the method is often indicated. Certainly, if internal fixation is to be used, the time-lag after injury should be short; the wound must have been débrided well; residual dead space in the wound must be at a minimum; and closure of the margins of the wound by suture must be feasible. If these requirements are not met, internal fixation is probably too hazardous. It would be preferable to use some other method of management and to direct all efforts toward obtaining wound healing, after which, open reduction and internal fixation, if indicated, may be carried out through an intact skin-envelope.

Summary

Open fractures demand prompt definitive management as emergencies. The objective of management of the wound is to prevent infection. Unless the surgeon can be sure that the depths of the wound have not been contaminated and that all tissue within the wound is viable, enlargement of the wound and a thorough débridement are indicated. The choice of the method of management for the fracture requires expert judgment. The fracture must not be ignored, and it must be reduced. Reduction of the fracture minimizes dead space and actually predisposes to wound healing, without infection. A septic fracture is usually an unreduced fracture. Because maintenance of reduction of the fracture and immobilization of the fragments are important deterrents to infection, internal fixation often is indicated as a part of wound management.

ACTIVE AND PASSIVE ANTITETANUS IMMUNIZATION

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The complete effectiveness against tetanus of the active immunization of persons, as produced by a series of tetanus toxoid injections, was thoroughly established by the experience of the armed forces of the United States during World War II. The sole qualification which must be attached to this statement, however, is of the utmost importance today to the practicing physician who must treat an acutely injured patient. In order to take advantage of this immunity, the physician must be certain that such a patient has previously been given an adequate course of toxoid injections. On the other hand, the protective value of tetanus antitoxin when adequate dosage is used has also been established by experience. The latter constitutes prophylaxis by means of passive immunization, but the method involves all the disadvantages and dangers of the administration of foreign protein. It is probably fair to say that there are few physicians who treat patients for injuries who would not be gladdened to learn of a safe substitute for tetanus antitoxin. If tetanus were a contagious disease comparable to smallpox, it is likely that public opinion would make active immunization compulsory for all persons. Only by a mass immunization program can the annual death toll from tetanus be wiped out. Despite the active efforts of many physicians to bring about mass immunization, they have not been successful; for the present, at least, the antitetanus measures must be suited to the person undergoing treatment.

Review of Causative Mechanism

In order to better comprehend the rationale of present methods, it seems worthwhile to review the facts. The clinical manifestations of tetanus result from the effects on the peripheral and central nervous system of the powerful toxin produced by the living bacillus, Clostridium tetani. This organism, a spore-bearing, strict anaerobe, is distributed widely throughout the world. It is found commonly in the feces of barnyard animals and birds (including pigeons), and it can also be found in human feces, although to a lesser extent. Little or no inflammation attends the growth of the bacteria in human tissues, and it appears that even the most trivial injury to living tissues may result in enough local damage so that the spores can develop into bacilli, which then begin to manufacture toxin. Tetanus toxin reaches the central nervous system either by way of a peripheral nerve trunk or through the bloodstream and has been demonstrated to be present in the blood 12 to 24 hours before the symptoms of tetanus become apparent. Tetanus toxin becomes fixed in the tissues of the central nervous system, after which such toxin can no longer be inactivated by antitoxin.

Prophylaxis

From these facts, it may be concluded that there could be, in theory, four entirely different methods of preventing clinical tetanus. The first and probably the best of these is the prevention of injury. The second method of prevention of tetanus is the proper treatment of the wound in order that anaerobic growth may not take place. The third theoretical prophylactic measure would be the use of agents, either chemotherapeutic or antibiotic, which prevent the growth and development of the bacilli. The fourth prophylactic method is, of course, the use of some means to neutralize or inactivate tetanus toxin. The latter measure is the subject of this discourse. Accordingly, it should be emphasized that immunization against tetanus, whether active or passive, is directed against tetanus toxin and not against the micro-organisms. If one remembers this point, it is easier to understand why immunization might fail to protect, since the bacilli might continue to grow and to produce toxin beyond the capacity of the immunizing substance to inactivate it.

It is of passing interest to mention that recovery from the disease does not produce immunity. There have been many reports of repeated attacks of tetanus in persons, and studies of the blood taken from patients who recovered did not show an antitoxin titer after an interval sufficient to permit excretion of the antitoxin given the patient therapeutically. The explanation for this probably lies in the fact that the amount of tetanus toxin which is lethal to a man is too small an amount to produce an immunity.

Passive Immunization

Tetanus antitoxin is prepared by injecting animals, notably the horse, with sublethal doses of tetanus toxin prepared from broth cultures of Cl. tetani or with tetanus toxoid. Tetanus antitoxin is then prepared from the blood serum of the immunized animal. One unit of tetanus antitoxin will protect a 350-Gm. guinea pig against about 1,000 lethal doses of tetanus toxin. It should be realized that it is not possible to state what constitutes a protective level of antitoxin in the human being because, obviously, the amount of toxin being produced by the micro-organisms is the deciding factor. It is intriguing to consider the complacency with which most physicians have, until now, administered 1,500 units of tetanus antitoxin, believing that the patient was thus protected. A single dose of 1,500 units of tetanus antitoxin, as commercially obtainable, will, if given intramuscularly, produce a gradually rising titer of antitoxin in the circulating

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blood which, by the fourth or fifth day, reaches a level of 0.1 unit of antitoxin per milliliter of serum. This level is maintained until about the 10th or 11th day when it begins to fall. By the end of the third week, there will usually be no demonstrable titer in the blood.

Not long ago, the records of all of the patients treated for tetanus in the general hospitals of Baltimore during a 25-year period were reviewed. Tetanus is not extremely common in Baltimore, as only seven or eight patients per year are treated. Records were found of 25 patients who had been given 1,500 units of tetanus antitoxin at the time of treatment of their original injury but in whom the symptoms of tetanus appeared, nevertheless. Of this group, 13 died of tetanus; thus, it would seem that these patients, at least, were not afforded adequate protection. It has been shown that an initial administration of comparable amounts of tetanus antitoxin to laboratory animals is not protective when lethal doses of live spores are introduced. It is the feeling of the majority of physicians working in this field today that any injured person who really needs tetanus antitoxin probably needs a larger dose than 1,500 units.

It has been stated that the commercially available tetanus antitoxin is, for the most part, prepared from the serum of the horse. Antitoxin prepared from bovine serum, however, is also available. A third and probably safer source of tetanus antitoxin is that obtainable from the blood of immunized persons. This has not been made commercially available as yet but probably should be because the complications of the administration of horse serum are disabling and dangerous. It behooves any physician who treats an injured person to consider carefully whether, in the individual circumstances, the danger to life is greater from tetanus or from the effects of the horse serum. Physicians familiar with the emergency rooms of large city hospitals have the uncomfortable impression that more and more of the population appear to be hypersensitive to horse protein. It is not necessary for a person to have had a previous injection of horse serum in order to develop hypersensitivity. This state can be acquired from exposure to horses or even, according to some authorities, from eating horse meat. A variety of consequences follows the injection of the horse serum. The most disastrous, of course, is the rather immediate occurrence of anaphylaxis and death. The more common complication is that of urticaria and serum sickness. I have not seen an accurate account of the human discomfort, disability, and mortality resulting from tetanus antitoxin, but there have been reports of damage to the central nervous system, including paraplegia, hemiplegia, and encephalitic manifestations of a lasting nature. As is well known to all physicians, any of these complications may occur, despite careful preliminary tests for sensitivity.

Active Immunization

Active immunization against tetanus was introduced by Ramon in 1925. As has already been mentioned, the biological perfection of this method was demonstrated during World War II, during which there was almost no occurrence of tetanus among the personnel of the armed forces of the United States. There was, however, a high incidence of this dread complication of injury among the troops of our enemies who were not actively immunized, especially in the islands of the Pacific. Although the authorities of the United States are not in full accord as to whether alum-precipitated toxoid or the fluid toxoid constitutes the most suitable antigen for the production of active immunity, it is, nevertheless, certain that two or three monthly injections of either preparation, followed some months later by a booster dose, will produce a lasting active immunity against tetanus toxin. It has been shown that this immunity persists for more than 10 years; high titers of antitoxin in the circulating blood are promptly recallable by a booster injection of toxoid. Hypersensitivity to tetanus toxoid is rare, although it does occur. Active immunization in such hypersensitive persons can be accomplished by intracutaneous injection of small amounts of the toxoid, with minimal risk. It must be pointed out, however, that there is an interval of at least 14 days between the first injection of toxoid and the appearance of significant amounts of antitoxin in the circulating bloodstream. On the other hand, when the person has received a previous course of toxoid injections, a booster dose produces a prompt recall, and the level of antitoxin is demonstrable within three or four days. Within seven days after such a booster dose in an actively immunized person, the level of antitoxin in the circulating blood will be quite high. Furthermore, this level remains for more than a year, far beyond the brief, temporary level produced by passive immunization.

The point must be again emphasized: Whereas active immunization with tetanus toxoid constitutes the best possible prophylaxis against tetanus, this method is of no use whatsoever in the treatment of a patient acutely injured unless that patient has already received his full immunizing course at some previous time. Currently under study are methods which, it is hoped, will result in the rapid production of active immunity; the certainty of these methods has not yet been established.

Comment

It is of interest to point out that there is a large, random experiment going on in the United States at the present time. It is well known that tetanus commonly complicates trivial wounds for which the patient does not seek medical aid. As a result, these patients first appear at a physician's office with full-blown tetanus. Furthermore, there is a growing reservoir in our population of persons who have had a basic course of active immunization but who have not had routine booster doses. Since 1950, many children in the United States have received tetanus toxoid, together with diphtheria toxoid, in infancy. There are also more than 15,000,000 persons in the nation who were immunized during their service in World War II, many of whom have probably had no booster dose subsequently. It should be possible in the next 5 to 10 years to gather a large body of information concerning the experience of these children and former armed services personnel for contrast with that of the rest of the population who are not immunized. This information will serve to prove whether immunity to tetanus toxin is of a lasting nature and whether booster doses are necessary at the time of injury.

Recent experimental work in the laboratory has shown that, if the course of therapy is begun at the time of injury, penicillin and broad-spectrum antibiotic agents such as tetracycline (Achromycin, Panmycin, Polycycline, Steclin, Tetracyn) hydrochloride are more protective against tetanus than are ordinary doses of antitoxin. These antibiotic agents appear able to prevent sporulation and growth of the bacilli, and, thus, no toxin is produced. There are two obvious points to be made concerning the use of antibiotics in this connection. The first and most important of these is that antibiotic agents do not neutralize tetanus toxin and, therefore, cannot be relied on to protect a patient in whom toxin is already being produced. The second point concerns the treatment of a patient who has tetanus. Antibiotic agents are quite useful in controlling the growth of the tetanus bacillus and, therefore, in reducing and possibly eliminating the source of the toxin when the source cannot be controlled by direct surgical means. If antibiotic therapy is used for prophylaxis, full dosage should be given for five to seven days.

There is, at the present time, a renewed interest in the subject of tetanus prophylaxis. This interest is due, in part, to the rather frequent occurrence of this complication of injury among patients in the southern states and to a growing abhorrence of the morbidity and mortality which are the consequences of widespread, routine use of tetanus antitoxin. Undeniably, the ideal solution to the problem is mass immunization of the population. Numerous county and state medical societies are already actively developing such programs. One of the unsolved problems of an immunization program concerns the identification of persons who have been immunized. It would seem to me that a good method for handling this problem would be to keep indexed immunization records of the population in state or county health departments so that a phone call or a telegram could produce the desired information promptly.

Summary and Conclusions

Until the day arrives when all of us have had active immunization to tetanus, however, each physician who treats injured patients must be ready to individualize the prophylactic measures against tetanus. The following steps are suggested as a guide: 1. Careful selection of patients for antitetanus measures is necessary. 2. Thorough cleansing and débridement of the wound must be done, in order to minimize the conditions favorable to anaerobic growth. At times, in large wounds with crushed tissues, this may involve leaving the wound open. 3. If the patient has been previously actively immunized (with a full course of tetanus toxoid), he should be given 0.5 cc. of fluid toxoid intramuscularly. 4. If the patient has not been previously immunized, he should be tested for sensitivity to horse serum, after careful questioning about such matters as previous injection or other allergic manifestations. Sensitivity testing is a medical responsibility and should not be delegated to nurses or other personnel. Both conjunctival and intracutaneous tests are useful. If the sensitivity tests are negative and if the physician has determined that the wound is one which may be complicated by tetanus, then tetanus antitoxin should be given; 5,000 units constitutes an adequate dose. The previous standard of 1,500 units should not be relied on as adequate. 5. If the patient has previously had antitoxin in horse serum or is sensitive to horse serum, bovine serum should be tried. There is still some controversy as to the virtues of administering antitoxin to a hypersensitive person. Under such circumstances, severe serum sickness is likely, and there is some doubt as to the duration of the passive immunity. If antitoxin is given to a hypersensitive person, it should be given carefully in graduated amounts and with the added precaution of having available epinephrine, antihistaminic drugs, cortisone (Cortisone, Cortogen, Cortone) acetate, and the equipment needed for the intratracheal administration of oxygen. Although this is generally called "desensitization," it does not render the patient insensitive to horse serum. 6. The use of penicillin or broad-spectrum antibiotics is indicated in persons who are extremely hypersensitive to horse and bovine serums and who are treated within an hour or two after injury. Full dosage of the agent should be given for five to seven days. 7. The treatment of an injury is probably an excellent time to begin the immunizing course of tetanus toxoid in those who have not previously been immunized. If this is done, however, care must be taken not to mix the toxoid and antitoxin in the same syringe nor to inject them in the same extremity, because one will inactivate the other. Separate syringes and needles and separate extremities should be used for each agent. 8. All physicians should take every opportunity to extend as widely as possible the benefits conferred by active immunization against tetanus.

PRELIMINARY COMMUNICATION

TREATMENT OF SHOULDER-HAND SYNDROME WITH GRISEOFULVIN

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and
William Kanenson, M.D., Philadelphia

When griseofulvin (Fulvicin) was made available for the treatment of fungus diseases, there was some question whether it was fungistatic or fungicidal. This became evident when fungus infections of the finger or toe nails were treated.[1] The growth was apparently inhibited by continuous treatment for a number of months, while an old nail was replaced by a new one. If treatment was discontinued before the new nail had completely appeared, the fungus would start growing again and the prior condition would return.

Since inflammation accompanying some fungus diseases of the skin [1] subsides rather abruptly, it was thought possible by us that griseofulvin might be another anti-inflammatory agent. Proceeding on this assumption, we decided to administer the drug to some of our patients with rheumatoid arthritis. Among the group of patients were a few with cases of shoulder-hand syndrome. The response in patients with rheumatoid arthritis was negative, while in patients with shoulder-hand syndrome it was remarkable.

According to Adams,[2] the shoulder-hand syndrome may be defined as a reflex neurovascular dystrophy affecting the shoulder and upper extremity, and provoked by a number of different causes. It is characterized by pain, tenderness, and limitation of motion of the shoulder, and usually aching, paresthesia, swelling, color changes, and limited mobility of the hands and fingers. Stiffness, weakness, muscular atrophy, and flexion deformity of the hand and fingers with trophic changes of the skin and subcutaneous tissues may develop in severe cases. Among the causes which are described are those which are predominantly vascular, such as Raynaud's disease and thromboangiitis obliterans; predominantly neurological, such as postherpetic herpes zoster and late hemiplegia; and others representing a combination of the two, such as cervical rib and scalenus-anticus syndrome. In some cases the cause cannot be determined. The disturbance is occasionally seen after severe myocardial infarction; here the mechanism is not understood.

After the clinical diagnosis of shoulder-hand syndrome had been made according to the above criteria, it was decided to administer 250 mg. of griseofulvin orally four times daily. With the discovery that the improvement was so dramatic, it was decided to substitute administration of placebos to help substantiate our findings. Accordingly, a placebo was made up to include all the markings and to look exactly like the original griseofulvin. At first the placebo was substituted. When there was a return of symptoms griseofulvin was again administered. Later, however, we believed that perhaps we might first administer the placebo for one week and then substitute the griseofulvin. This has since been done, with good results.

Report of Cases

CASE 1.—The patient was a 59-year-old woman with no antecedent history of cardiovascular accident or acute myocardial infarction. She first complained of pain in the right shoulder and hand in February, 1959. The onset was gradual. She was seen in the orthopedic clinic in April of the same year, when the diagnosis of bicipital tendinitis was made. Treatment at one to two-week intervals consisted of local injections of procaine and hydrocortisone with only temporary and variable success. Phenylbutazone had been given without benefit.

In November, 1959, the patient was referred to the arthritis clinic. The examination revealed a patient with pain and swelling in the right hand and pain and limitation of motion of the right shoulder. She was unable to abduct the arm beyond the level of the shoulder without excruciating pain. Forward motion was more limited. The hand was swollen, and the fingers could not be flexed to more than 50% of normal. It was tender and forced flexion caused severe pain. Pain radiated up to the right side of the neck and down the entire right arm. It was particularly annoying, so that the patient suffered many sleepless nights.

Griseofulvin, 250 mg., was orally administered every six hours day and night. Improvement was marked after the second day. At the end of two weeks, the patient was able to move the arm in all directions, but the hand, while its condition was much improved, still had some limitation of motion and swelling. Sleep was now uninterrupted.

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For the second week of therapy, a placebo was substituted for griseofulvin. At the end of this period, the patient was still feeling fairly well. She could move the arm in all directions without discomfort, and the condition of the hand was about the same as it had been the previous week. The placebo therapy was continued.

At the next visit, the patient stated that during the week, the pain had begun to return in the shoulder and hand. Sleep was again interrupted because of pain and, while she was not as distressed as she had been before treatment, she felt that all her symptoms were returning. Griseofulvin was again administered, and, after another week of this therapy, there was again marked improvement. Administration of the drug was continued and, at this writing, the patient is asymptomatic except for slight limitation of motion and slight swelling in the fingers.

Case 2.—A 78-year-old male patient was known to have had gouty arthritis for at least five years. He also was known to have osteoarthritis of the knees and hips. There was a history of myocardial infarction some years previously. The patient was sent to the arthritis clinic for evaluation.

In addition to the above findings, there was the complaint of continuous pain in the left shoulder radiating down the arm to the left hand. The hand was swollen, and motion in the fingers was limited. Any attempt to raise the left arm was painful and its motion was limited. The patient stated that he thought that he had had a stroke. He had complained of pain in the left arm for more than six months. Reflexes were normal.

Blood uric acid levels were above 6 mg.%. Administration of colchicine in therapeutic doses was of no avail. Three electrocardiograms, taken from April, 1958, to the present, confirmed the presence of an old anteroseptal myocardial infarction.

Griseofulvin, 250 mg. every six hours, was administered orally. After one week's medication, the patient returned to the clinic to state that the pain in the arm and hand had disappeared and that the swelling in the hand was reduced by about 50%. He had a great deal of motion in the arm, which had not been previously present. Administration of a placebo, to be taken every six hours, was substituted for one week. At the next visit to the clinic one week later, there was some return of pain and swelling in the hand. Pain was also returning in the shoulder and arm, and there was evidence of lessened motion in the arm to extension and abduction. Continuation of griseofulvin therapy again brought relief. After a few weeks of therapy, the patient was free from discomfort in the shoulder and hand. Swelling gradually disappeared from the hand, and finger movement gradually returned to normal. Administration of griseofulvin has had no effect on the osteoarthritis of the knees or hips.

Case 3.—A 50-year-old male patient's chief complaint was that of pain in the right shoulder radiating down the arm, with pain and swelling in the hand. The condition had developed gradually about one year previously. He had had numerous injections of dexamethasone around the shoulder joint, without success.

Examination showed swelling of the right hand, with limitation of motion in the fingers. Active movement of the arm was limited and caused considerable discomfort. On Jan. 8, 1960, the patient was given griseofulvin-placebo to be taken every six hours day and night. This therapy was continued for three weeks without improvement in the patient's condition. On Jan. 29, medication was changed to griseofulvin every six hours. There was improvement in a few days, and at each visit the patient stated that his arm and hand gradually were returning to normal. On one occasion, a placebo was substituted for one week, with a gradual return of signs and symptoms. The patient now takes griseofulvin in the dosage stated above and, at this writing, his condition is markedly improved.

Thus far, we have treated only 12 patients whose symptoms were in the category of shoulder-hand syndrome. There were six patients whose disease could have been idiopathic, three postcoronary and three posthemiplegic.

Comment

We are unable to give a scientific explanation for our findings. The consistency with which the improvement occurs is indeed unusual. We do not believe that griseofulvin is an anti-inflammatory agent. We have attempted to determine whether it is a uricosuric agent; in our series of cases, it has failed to reduce the blood uric acid level in a number of patients with hyperuricemia.

Summary and Conclusions

Twelve patients, whose disease, according to our interpretation, was in the category of shoulder-hand syndrome were benefited by the administration of griseofulvin (Fulvicin). Placebos, made to look identical to griseofulvin tablets, were substituted at varying intervals. These cases included postcoronary, posthemiplegic, and idiopathic shoulder-hand syndrome. This is a preliminary report in the hope that others might use this method to either confirm or refute our findings.

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The griseofulvin used in this study was supplied as Fulvicin by the Schering Corporation, Bloomfield, N. J., through Drs. George Babcock and G. K. Hawkins.

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NEWER CONCEPTS IN BACTERIOLOGY

THE presence of unusual forms in bacterial cultures has been recognized for many years. Such organisms, which were called pleuropneumonia-like (PPL), were the center of considerable controversy and were thought at one time to be causal agents in various diseases. Morphologically, these organisms differed so strikingly from bacteria that they were classified as an independent order or even in an independent class.[1] In 1935 Klieneberger[2] isolated from cultures of Streptobacillus moniliformis organisms which resembled bovine pleuropneumoniae and designated them as L 1. Originally it was thought that such organisms were distinct from S. moniliformis and lived in symbiosis with this organism.

In recent years the error of this view has been recognized, since similar forms of many micro-organisms have been identified. It is now known that culture of many micro-organisms under various conditions, such as in the presence of antibiotics, other bacteriostatic chemicals, phage, and antibodies, results in the formation of L forms. Since the original observations it has been repeatedly shown that culture of a number of gram-negative and gram-positive bacteria in the presence of penicillin results in the formation of organisms similar to L forms and protoplasts.

The understanding of this phenomenon has come about as a result of several independent lines of investigations. Chemical investigations, particularly those of Salton and co-workers, have been concerned with the chemical composition of bacterial cell walls. It has become apparent that bacteria contain a cell membrane, now called the protoplast membrane, comparable to mammalian cells. However, the resistance of bacteria to osmotic changes and mechanical stress depends on the fact that this membrane is encased in a more rigid cell wall material. The composition of cell wall material is unique in that it contains a limited number of amino acids, including D-forms of several amino acids, α-ϵ-diaminopimelic acid and a lactic acid ether of N-acteylglucosamine (muramic acid) as well as acetylglucosamine. In gram-negative organisms the structure is more complex. Some organisms also contain polyalcohol phosphates. In certain bacteria other substances appear to be part of the cell wall structure. It is notable that in streptococci the group-specific polysaccharide makes up a major portion of the cell wall.

The interrelationship between bacterial L-forms, PPL organisms, and the parent micro-organisms has been clarified by the observations of Weibull[3] that treatment of Bacillus megatherium cells with lysozyme in a suitable medium produces spherical forms which have been called bacterial protoplasts. Such forms are readily lysed by osmotic shock. Since chemical and morphologic evidence indicates that lysozyme acts by dissolution of cell wall substance, it becomes apparent that bacterial protoplasts may be regarded as bacterial cells denuded of cell wall material. Chemical analyses have also shown that L forms are deficient in cell wall material. In view of their known osmotic fragility, the close relationship between L forms and protoplasts seems apparent. In the case of L forms synthesis of cell wall material is inhibited, while treatment with lysozyme results in removal of preexisting cell wall material. It has been suggested that the term protoplast be reserved for forms in which the absence of all cell wall material has been demonstrated.

Recent studies have made considerable progress in the elucidation of the physiology of protoplasts derived from group A streptococci. Maxted[4] and Krause[5] found that an enzyme induced by phage in group C streptococci removes the cell wall of group A streptococci. Freimer and co-workers[6] showed that under special conditions the resultant osmotically sensitive protoplasts may be cultured in the presence of penicillin and high salt concentration. Such protoplasts are capable of synthesizing M protein, the type-specific antigen of group A streptococci. When such protoplasts are cultured in the absence of penicillin, reversion to the parent organism occurs, a phenomenon well known for L forms of a number of micro-organisms.

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Elucidation of the action of penicillin has resulted from the original observations of Park[7] who discovered that culture of staphylococci in the presence of penicillin results in the accumulation of a series of uridine nucleotides. It has been demonstrated that these contain muramic acid and a limited number of amino acids. More recently, Strominger and co-workers[8] showed that the amino acid composition of one of these nucleotides corresponds to that of the cell walls of staphylococci. It was concluded that penicillin acts by blocking the synthesis of cell wall.

Although much remains to be learned about the chemistry and biosynthesis of bacterial cell walls, a pattern of considerable significance seems to emerge from all of these studies. It is apparent that bacterial forms with various aberrations of or absence of cell walls may be obtained. Such forms resemble animal cells in their sensitivity to osmotic changes. For this reason they are not readily cultured under the usual conditions of bacterial techniques. The role of such forms in human disease is worthy of reexamination. The possibility exists that such bacterial forms may be present in tissues and go unrecognized by conventional culture techniques.

ANTIBIOTIC-RESISTANT STAPHYLOCOCCI

Studies in many parts of the world revealed several years ago that more than half the strains of Staphylococcus aureus isolated from hospitalized patients were resistant to penicillin, streptomycin, and the tetracyclines. This led to the fear that staphylococcic infections would become untreatable because of the development of resistance to each new antibiotic as it appeared. The relationship between use of various antibiotics and the amount of resistance that would develop was not known, and studies along this line have been awaited with interest.

In an article in this issue, Bauer and co-workers have reported definite differences in resistance of staphylococci to commonly used antibiotics in relation to the number of kilograms consumed per year in a general hospital. Particularly striking was the fact that a relatively small percentage of strains develop resistance to chloramphenicol, despite the consumption of large amounts of this antibiotic. Similar results have recently been reported by Fisher.[1] The failure to develop a higher percentage of chloramphenicol-resistant staphylococci is due in part to the emergence of fewer resistant mutants to this antibiotic, but it may also be attributable to rapid back-mutation of resistant strains to susceptibility and to the replacement of resistant bacteria by sensitive strains. Chloramphenicol-resistant strains would appear to be genetically unstable, with a decreased ability to survive when competing with other strains in the absence of the drug.

Administration of two antibiotics simultaneously has been widely practiced in the treatment of staphylococcic infections, in an attempt to prevent the emergence of drug-resistant organisms. Chloramphenicol and erythromycin represent the most widely used combination in the hospital where the studies of Bauer and co-workers were carried out. Despite the use of large amounts of these two drugs in combination, it is of interest that the incidence of resistant staphylococci has gradually increased to only 20% for chloramphenicol and 30% for erythromycin. Only 16% of strains were resistant to both antibiotics and almost all of these strains were also resistant to penicillin, tetracyclines, and streptomycin. Barber and co-workers,[2] in England, observed what they interpreted to be cross-resistance between erythromycin and chloramphenicol and no longer advocate use of this combination. The results of Bauer and co-workers do not support the concept that cross-resistance occurs commonly between these two antibiotics.

The other principal method used to combat the development of antibiotic-resistant staphylococci has been an attempt to restrict antibiotic usage, and specifically to withhold certain antibiotics altogether except under special circumstances. In a recent study reported by Barber and co-workers,[3] restriction of penicillin led to a reduction in the incidence of hospital-acquired infections due to resistant staphylococci and an increase in the number of infections due to penicillin-susceptible strains. Studies of this sort are of great interest but do not settle the question whether restriction of various antibiotics should be a routine policy in hospitals. It is rather doubtful whether, aside from use of antibiotics only where they are actually indicated, the restriction of any one or a group of antibiotics is necessary at present. When the infecting organisms are resistant to penicillin, streptomycin, and the tetracyclines, as they commonly are, the physician still has the following agents to choose from: vancomycin, ristocetin, erythromycin, chloramphenicol, kanamycin, novobiocin, triacetyloleandomycin, and furaltadone. For milder infections, it should always be possible to select two antibiotics which can be taken simultaneously by mouth with minimal difficulty. For the more serious infections, vancomycin[4] given alone by the intravenous route has proved effective. To date, after it has been used on a fairly large scale for more than three years, strains of staphylococci resistant to vancomycin have not been encountered.

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ARABIC MEDICINE

Although Islamic culture dominated the eastern and western worlds for more than 10 centuries, there was a paucity of medical literature prepared during this long span of history. One is not justified, however, in drawing the obvious conclusion that this implies a sterility of medical culture or an impoverishment of the art of medicine; quite the contrary. Many important observations were made in the medical sciences; the physicians of the Middle Ages bridged the gap in medicine between the classical period and the Renaissance as effectively as did the leaders in other intellectual disciplines. The Arabs translated the Greek texts into their language and pursued independent scientific investigations.

Since few Arabic words or roots remain in modern medical usage, medical history allocates proportionately little emphasis to the writings and achievements of this thousand-year period. One small step to correct this deficiency has been taken by Prof. M. Z. Siddiqi of Calcutta University, who has, at long last, published his "Studies in Arabic and Persian Medical Literature."[1] The manuscript was essentially completed and ready for publication in 1925, according to the author.

The preeminent physician of the most productive era of Arabic medicine was 'Alí ben Rabban. He was born not later than 810 A.D. His famous medical compendium *Firdausu 'l Hikmat* (The Paradise of Wisdom) was completed before he reached the age of 40 years. Of the four copies of *Firdausu 'l Hikmat* that are extant, it may be unnecessary to note, one is in the British Museum.

Arabic medical literature preserved the achievements of the Greeks and correlated them with the writing and texts of the Egyptians, Persians, Chinese, and Asiatic Indians, cultures which were mingled with the Arabic over the long span of time. The Arabic physicians taught by means of the case system. Their individual experiences in hospitals and consulting rooms were collected throughout the Moslem world from Algeria to India. Several case histories are given in Siddiqi's appendix that date from the ninth century. The physical findings on a man with a substernal aneurysm are recounted. There are two instances of epilepsy and at least one example of tuberculosis of the hip.

Several notable contributions to the progress of medicine may be documented. The three ossicles of the ear were described and assumed to be responsible for the sense of hearing. Sugar was recognized as a constituent of blood. The three structural layers that make up the wall of blood vessels were described. The fabric of the brain was thought to be similar to that of peripheral nervous tissue. The germ theory of disease and the suggestion that close contact might spread contagion was recorded. The association of exophthalmos and goiter was recounted in a document in the 12th Century. Another remarkable physician, ar-Rází (865 A.D.), is believed by Siddiqi to be a strong contender for the honorific, "Father of Pediatrics." He anticipated the conditioned reflex theory of Sherrington. Arabian physicians used the stomach tube for the treatment of poisoning and prescribed whole liver for the treatment of diseases of liver. The application of cautery for hemorrhage was practiced as well as tracheotomy. Lenses were provided for defective vision, while cataracts were attributed to opacity of the lens.

Hospitals were among the great glories of Islamic culture. These included permanent hospitals and mobile hospitals, with physicians, surgeons, and assistants in attendance. The first large hospital was constructed in 707 A.D. More than 60 hospitals were reported in one community in 1160 A.D. When a poor patient was discharged from the hospital he was given money enough to provide him with food for a time. Medical schools were attached to some of the hospitals. The earliest mobile hospital was organized in 942 A.D.

Siddiqi provides a list of medicaments and diseases in the appendix. The Arabic term for gout is al-Niqras. I suspect that Colchicum, which was a recognized drug for the treatment of gout in the 12th century, may be the Arabic al-'Urýqul-Sufr, or Curcumae Longae Radix.

No center of Moslem medicine persists in Asia Minor today. The influence, nevertheless, of the culture that flourished for a longer time than any recorded is so diffused that for most of us the importance and magnitude of the contributions may be noted with profit.

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EARLY MANAGEMENT OF ACUTE TRAUMA

The objectives of treatment in trauma are to save life, to save limb, and to promote healing so that with or without reconstructive surgery at an elective time the patient will resume his normal activities without handicap and with minimum loss of time. In this issue of THE JOURNAL is a symposium on the early management of acute trauma. Careful study of the individual papers will provide the physician with certain fundamental principles to guide him in reaching the stated objectives.

At the outset, it is well to warn that even so-called basic principles are subject to change, and the minute details of treatment certainly change as new knowledge displaces the old. Therefore, to meet his obligations, the physician must keep abreast of advances in our understanding of the problems of trauma and of improvements in the methods of treatment. Indeed, this is the central problem of medical education. One cannot teach principles and details of medicine which are to last a lifetime. In a successful curriculum the student and physician will have learned that his is the responsibility to acquire new facts, to discard outmoded ones, to modify his "basic" concepts, and to learn new techniques.

In keeping with these thoughts, the Council on Drugs of the American Medical Association sponsored this symposium to be held in close collaboration with a medical school and with the local medical organizations which play an important part in the postgraduate education of the physician. The participants in the symposium consider the management of the patient who has incurred trauma from several points of view. Beecher emphasizes the nice distinction between "suffering" and "pain," a matter of practical importance, for despite the lessons learned in World War II, morphine is still injudiciously used in trauma. The size and appearance of a wound bears little relation to the severity of the pain it can produce. The "suffering" which a patient experiences as the result of injury is an interpretative phenomenon and can be relieved much less dangerously by a sedative than by a narcotic. The administration of morphine can be both useless and life-endangering, especially for the injured patient in shock.

Hemorrhage and lesions which interfere with pulmonary ventilation must be treated as emergencies which threaten life itself. The lacerated and obstructed trachea and bronchus, the massive atelectasis, the simple and the tension pneumothorax must be recognized and treated aggressively. Bleeding into certain areas has particular significance, such as that from the middle meningeal artery or within the pericardium. These require prompt recognition and urgent treatment. The hemorrhage of ordinary trauma is not such a dire emergency as these, but it results in progressive hypotension, inadequate perfusion of tissues and vital organs, and increasing deterioration of the organism if the hemorrhage is not stopped and the deficit in circulating blood volume corrected. These problems are well discussed by Howard, by Artz, and by Seeley. The biological effects of oligemia are dynamic rather than static. In trauma, they are usually best reversed by the administration of whole blood. In the symposium are described exceptions to this general rule, and the use and abuse of substances other than whole blood are discussed.

The early management of burns has been under close scrutiny during the past two decades. It is recognized that at least a part of the reallocation of body fluid which takes place immediately after a severe burn has been incurred is transitory. Thus, when this acute phase is over, the patient must handle not only the later effects of the burn but also the material used in treating the early phase of the injury. With this as a thesis, Wilson and Stirman state that "the essence of safe treatment for shock that attends burns is the replacement of the extracellular fluid losses. A balanced salt solution resembling the ionic composition of extracellular fluid can be given by mouth or by veins." Blood and colloidal solutions are reserved for very special indications. The reader will find careful study of this paper both exciting and rewarding.

A common, and often disastrous, error committed in the management of open wounds is the practice of sealing devitalized tissue, foreign bodies, and bacteria beneath nicely sutured skin. The patient goes elsewhere for treatment of the infected sutured wound or to die of tetanus. The approach to the management of the open wound is clearly described in this symposium. It should further be emphasized that, especially in the case of the explosive wound, it is impossible to sterilize it and to be certain that the remaining tissue is viable. Four to six days after the débridement, however, the infected or nonviable tissue can be clearly recognized and excised before the wound is closed.

Altemeier and Wulsin present in detail the manner in which antibiotics can serve as adjuvants in the treatment of wounds of violence. They discuss the role of these agents in the prevention of infection in contaminated tissue and in the treatment of established infection, including "septic shock." It is worth emphasizing that, while these substances have been of inestimable value in the treatment of injury and disease, no amount, kind, or combination of antibacterial agents can take the place of sound surgical judgment.

Altemeier and Wulsin also clarify the role antibiotics can play in the prevention and treatment of clostridial infections. The experience with wounds during World War II demonstrated beyond doubt the effectiveness of active immunization with toxoid. Interestingly, persons who have recovered from tetanus are not immune to the disease. On the contrary, high titers of antibody are obtainable in actively immunized human subjects, and more thought should be given to the preparation of antitoxin from the serums of such persons. Stafford presents a guide for questions of immunization against tetanus when dealing with accidental wounds. In general, the formerly recommended dose of antitoxin for passive immunization is too small. If needed at all, it would be better to administer 5,000 units, rather than 1,500, and even higher doses for more extensive and serious wounds. When the patient's status with regard to immunization is not known, passive immunization is administered along with a first injection of toxoid to serve as a "booster" in case the patient had been previously immunized. The same procedure can be followed for the patient known to have had no immunization. These substances must be administered through separate syringes and at different sites. Universal active immunization would solve many of the problems the physician must face in treating accidental injuries.

Wounds associated with fractures present certain special problems because of the peculiarities of bone and the manner in which it heals, but the general principles of wound management remain the same. These are clearly described by Hampton in his essay. Wisely, he stresses the importance of early reduction and fixation of fractures—as early as is consistent with the general principles of wound management. Quite rightly, he also stresses the importance of emergency splinting in fractures of the long bones. Not only is pain relieved thereby, but also the bone fragments cease inflicting additional injury by their motion during transportation.

The transportation of the injured prior to emergency surgery is well described by Artz, by Seeley, and by Hampton. It is well for doctors to consider problems of transportation after as well as before surgery. The inadvisability of transporting the patient with a severe wound of the extremity before the 5th to 7th postoperative day, or the patient who has had laparotomy for serious visceral injury before the 7th to 10th postoperative day, is well known. This practice, of course, cannot always be followed, but examples of the dire results of having to break this policy are numerous.

The responsibility for the welfare of the patient who has incurred trauma should be in the hands of a surgeon whose background and interests permit him to look on the patient as a whole person instead of a "fractured femur." Artz has made a point of this in his paper. Patients who have been injured often have multiple injuries. The surgeon in charge must determine the relative importance of the various injuries and assign priorities for their treatment. He must obtain the help of specialists for solving problems which lie outside his own field of competence. He must have sufficient experience with the behavior of patients who have been injured to recognize that occult problems may exist when things are not going well, and he should aggressively seek them out. In fact, an injured person may have only a solitary injury but he may have other problems of equal or greater importance, such as obstruction to the outlet of the bladder or carcinoma of the gastrointestinal tract. Thus, the surgeon in charge should be a good doctor; he could well be a specialist.

THE SOPORIFIC SPONGE AND SUBLIMATES

The composition of a savour to be made by surgeons, according to Master Hugo, is as follows: take of opium, and the juice of unripe mulberry, hyoscyamus, the juice of spurge flax, the juice of leaves of mandragora, juice of ivy, juice of climbing ivy, of lettuce seed, and of the seed of the lapathum which has hard, round berries; and of the shrub hemlock, one ounce of each. Mix these all together in a brazen vessel, and then put into it a new sponge. Boil all together out under the sun during the dog days, until all is consumed and cooked down into the sponge. As often as there is need, you may put this sponge into hot water for an hour, and apply it to the nostrils until the subject for operation falls asleep. Then the surgery may be performed and when it is completed, in order to wake him up, soak another sponge in vinegar and pass it frequently under his nostrils.—The Surgery of Theodoric, vol. 2, books 3 and 4, translated by E. Campbell, M.D., and J. Colton, M.A., New York, Appleton-Century-Crofts, Inc., 1960, pp. 212-213.

THE CORRECT WORD

Whatever be the thing one wishes to say, there is only one noun to express it, only one verb to give it life, only one adjective to qualify it. We must search, then, till that noun, that verb, that adjective, are discovered; never be content with an approximation, never resort to tricks, however happy, or to buffooneries of language, to avoid a difficulty . . . There is no need of the eccentric, complicated, multifarious sort of Chinese vocabulary, which is inflicted on us at the present day under the name of artistic writing, to enable us to describe every shade of thought; but it is necessary to discern, with the utmost lucidity, all the modifications of the value of a word according to the position it occupies. Let us have fewer nouns, verbs, and adjectives with almost incomprehensible meanings, and more varied phrases, differently constructed, ingeniously turned, sonorous and full of skilful rhythms. Let us endeavor to be excellent stylists, rather than collectors of rare terms.

It is, in fact, more difficult to turn a phrase to suit one's self, to make it say everything (even that which it does not express), to fill it with hidden meanings, and with secret suggestions which are not formulated, than to invent new expressions, or to seek in the depths of old forgotten books all those that are obsolete and have lost their significance, and for us are only dead words.—G. de Maupassant, Pierre and Jean, Translations, Critical and Interpretative Essays by Alfred de Sumichrast, Ph.D., and Adolphe Cohn, M.A., LL.B., New York, A. L. Burt Company, 1917, pages 16-17.

MEDICAL NEWS

COLORADO

Dr. White to Head Preventive Medicine Department.—Dr. Kerr Lachlan White, associate professor of preventive medicine at the University of North Carolina School of Medicine, Chapel Hill, will become professor and head of the department of preventive medicine at the University of Colorado School of Medicine, Denver, on July 1. Dr. White received his M.D. degree from McGill University Medical School in 1949. He joined the faculty of the University of North Carolina Medical School as assistant professor of preventive medicine in 1953 and was made associate professor in 1957. Under Dr. White's leadership, it was announced, it is expected that the C. U. department of preventive medicine will be reorganized, both in respect to its teaching and research programs.

Personal.—John J. Conger, Ph.D., head of the division of clinical psychology, University of Colorado School of Medicine, Denver, was appointed to a three-year term as chairman of the research committee of the President's Committee on Traffic Safety.——Dr. C. Wesley Eisele, assistant dean in charge of postgraduate medical education for the University of Colorado School of Medicine, Denver, is the new president of the Commission on Professional and Hospital Activities, Inc., a service organization for hospital staffs which provides member hospitals with information for improving treatment and care. Headquarters of the organization are at Ann Arbor, Mich. The organization has 137 member hospitals, and is sponsored by the American College of Physicians, American College of Surgeons, and American Hospital Association.

Program for Students on Readiness for Medicine.—"Preparation for Medicine" was the theme of a one-day program for more than 150 college and university students from the Rocky Mountain area who were guests of the faculty of the University of Colorado School of Medicine on Saturday, May 14. Premedical students from Colorado and neighboring states, with their faculty advisors, met on the Medical Center campus for the affair, held annually to provide counseling for collegians planning careers in medicine. The visitors were welcomed by Dr. Robert J. Glaser, vice-president for medical affairs and dean of the school, and by Dr. Reginald H. Fitz, associate dean. A lecture and demonstration period, luncheon with members of the faculty, a panel discussion on the requirements for admission to medical school, and a tour of the School of Medicine and Colorado General Hospital comprised the program.

DISTRICT OF COLUMBIA

Meeting of Former Hospital Staff Members.—The first William Alonza Warfield Award for distinguished service by a former intern or resident of Freedmen's Hospital will be presented to Dr. Peter Marshall Murray, New York surgeon and member of the Howard University board of trustees for 36 years, at the 38th annual meeting of the Association of Former Internes and Residents of Freedmen's Hospital to be held at the Howard University College of Medicine, June 7-9. On June 6 a golf tournament is planned. Dr. William Earle Matory, chief resident in surgery at the hospital, will be presented the first Daniel Hale Williams Award for "outstanding achievement during the past year." One of the founders and the fourth president of the association, Dr. Murray is a past-president of the National Medical Association. Dr. Luther O. Baumgardner, Cleveland, will be installed as the 39th president at the close of the three-day meeting.

ILLINOIS

Institute for Rehabilitation Personnel in Carbondale.—An Institute for Rehabilitation Personnel will be offered by the Rehabilitation Institute of Southern Illinois University June 19-July 1 in Carbondale. The institute is designed for workers engaged in either rendering direct service to the handicapped or in organizing the community to recognize and assume its responsibility for the handicapped. Special emphasis will be placed on a coordinated approach in the rehabilitation process. The program is arranged under the following general headings:

General Orientation
Scope of Rehabilitation
Theory and Dynamics of Behavior
The Rehabilitation Process
Problems of the Handicapped
Professional Responsibilities in Rehabilitation
Sequences of Rehabilitation Services (two days)
Pertinent Therapeutic Approaches in Rehabilitation
Organizing Communities for Rehabilitation

The institute is partially supported by a training grant provided by the Office of Vocational Rehabilitation, Department of Health, Education, and Welfare, Washington, D. C. For information, write the coordinator for the institute, Guy A. Renzaglia, Ph.D., Director, Rehabilitation Institute, Southern Illinois University, Carbondale, Ill.

Physicians are invited to send to this department items of news of general interest, for example, those relating to society activities, new hospitals, education, and public health. Programs should be received at least three weeks before the date of meeting.

Chicago

Hospital Expansion Program.—On May 2, the South Chicago Community Hospital broke ground for a 2-million-dollar expansion program. The financing of a 72-bed addition has been consummated and construction will be planned for occupancy by Dec. 31, 1961. Dr. Antonio G. Cesare, president of the medical staff, and Dr. Yngve Joranson, chief of staff, participated in the ceremonies. The hospital, opened in 1905, will have a total of over 300 beds.

Dr. Bauer to Receive Honorary Degree.—Announcement has been made that Dr. William W. Bauer, Director, Department of Health Education, American Medical Association, and former editor of *Today's Health*, will receive an honorary doctor's degree "in recognition of his long and distinguished service in the fields of health and medicine as well as other constructive enterprises." The degree is to be conferred by the George Williams College of Chicago at its Commencement on Sunday, June 5.

Hospital Alumni Meeting.—The Michael Reese Hospital Alumni reunion will be held on Friday, June 10. There will be a luncheon and open house throughout the day at Michael Reese Hospital, and a banquet at the Furniture Club in the evening (cocktail party at 6:30 p. m., dinner at 7 p. m.). Former house staff and present attending staff members are urged to make their reservations at once. Write to Michael Reese Hospital Alumni Association, 29th Street and Ellis Avenue, Chicago 16.

Exhibit for Hospital Month.—A new exhibit opened May 8 at the International College of Surgeons' Hall of Fame, 1524 Lake Shore Drive. Called "The Functional Hospital," it will be on view for a month to coincide with National Hospital Month. After that, the exhibit will go on a tour of member nations of the society. The exhibit is open to the public. Features include a hospital room of the future; a table model of the unique "survival complex" of the Southwest Texas Methodist Hospital, San Antonio; table model of St. Joseph's Hospital, Belvidere, Ill.; exterior and floor plan paintings of the Hotel Dieu Hospital addition, New Orleans, which incorporates a new circular operating room arrangement; photographs and blueprints of the new Mount Sinai Hospital, Milwaukee; paintings and floor plans of the new oriental "hospital in the desert" in Jerusalem, Jordan; and the modern extensions to Little Company of Mary Hospital, Evergreen Park, Ill.

Dr. Vail Receives Sight Conservation Award.—The Leslie Dana Gold Medal Award for "meritorious work in the field of sight conservation and prevention of blindness" was presented May 5 to Dr. Derrick T. Vail, head, department of ophthalmology, Northwestern University Medical School. The presentation was made by Dr. Leslie C. Drews, a member of the executive committee of the Lighthouse for the Blind and the St. Louis Society for the Blind at a dinner which was jointly sponsored with the St. Louis Ophthalmological Society in St. Louis. The Leslie Dana Award is the symbol of "highest achievement for an individual whose efforts have contributed to mankind's struggle against the causes of blindness." Dr. Vail becomes the 34th recipient of the award since it was established in 1925 by the late Leslie Dana, businessman of St. Louis. A member of the board of directors of the Illinois Society for the Prevention of Blindness, Dr. Vail is the holder of the Outstanding Contribution Medal, Section on Ophthalmology, American Medical Association, 1956, and the Doyne Lecture and Medal, Oxford Ophthalmological Congress, 1957.

KANSAS

Traveling Professorship in Pathology Established.—A traveling professorship in geographical pathology has been established for Dr. John F. Higginson, of the department of pathology and oncology, University of Kansas Medical Center, Kansas City. Designated the Lewis and Hubbard Traveling Professorship of Geographical Pathology, in honor of two benefactors of the University of Kansas, the appointment is effective July 1. Prior to joining the University of Kansas faculty in March, 1958, Dr. Higginson was head of the geographical pathology unit of the South African Institute for Medical Research in Johannesburg. He is a consultant pathologist in the World Health Organization, and a member of the geographical pathology committee of the International Union Against Cancer. Dr. Higginson will continue his teaching and research interests on campus but also will be responsible for developing cooperative research in geographical pathology between the University of Kansas and medical institutions abroad.

MARYLAND

Dr. Rich Awarded Trudeau Medal.—Dr. Arnold Rice Rich, emeritus professor of pathology, Johns Hopkins University School of Medicine, Baltimore, was awarded the Trudeau Medal of the National Tuberculosis Association May 16. The medal is awarded annually for distinguished service in the field of chest diseases. Author of "The Pathogenesis of Tuberculosis," Dr. Rich obtained his medical degree in 1919 from Johns Hopkins, with which he has been associated throughout his professional life. He was named Baxley Professor and director of the department of pathology of Hopkins in 1947 and served in that capacity until 1958, when he became emeritus professor.

MASSACHUSETTS

Dr. Lennox to Be Honored.—Dr. William G. Lennox is to be honored at a dinner in Boston on Sunday evening, June 12, 7:15 p. m., at the Harvard Club. The occasion, called "An Evening with Dr. Lennox," commemorates his 38 years of practice and research in the field of epilepsy, and coincides with the publication of his new two volume work, "Epilepsy and Related Disorders." There will be a cocktail hour from 6 p. m. to 7 p. m., immediately preceding the dinner. The American Epilepsy Federation is sponsoring this event.

Plan Building for Nutritional Research.—Informal ground-breaking ceremonies at the site of a new three-level nutritional research building to be erected by the Harvard School of Public Health were held May 9 at Huntington Ave. and Wigglesworth St., Boston. Construction is expected to start in the fall. The new nutritional research building, where biological and medical sciences will be applied to human nourishment and its relation to heart disease, obesity, and other health functions, was made possible through a gift of $102,600 a year for 10 years from the General Foods Corporation. An additional grant from the National Institutes of Health (U. S. Department of Health, Education and Welfare), Research Facilities Branch, in the amount of $529,000 has been awarded for financing the construction of the building. The nutritional research building will be erected adjacent to a second new research structure, to house the school's newly created division of environmental hygiene which includes the Guggenheim Center for Aviation Health and Safety.

Institute on Emotionally Disturbed.—A two-week Institute on the Rehabilitation of the Emotionally Disturbed will be conducted by Boston University's School of Education, beginning Monday, June 20, during the university's summer session, according to an announcement by Julian S. Myers, Ph.D., coordinator of rehabilitation counseling and associate professor of education. The role of the vocational counselor in the psychiatric setting, including his relationship to other professional personnel and various state administrations, will be the focal point of the institute. Practical aspects of setting up a closer working relationship between state hospitals and state divisions of vocational rehabilitation will also be stressed. The university's third annual Institute on the Rehabilitation of the Emotionally Disturbed will be offered as a three-credit course open to individuals employed in psychiatric rehabilitation. Professionals within this area include counselors, psychiatric social workers, psychologists, psychiatric nurses, educators, physicians, and administrators in the psychiatric setting. A limited number of stipends covering costs relative to the institute are available. The institute is being sponsored by the United States Office of Vocational Rehabilitation. Requests for application forms should be addressed to Dr. Julian S. Myers, School of Education, 332 Bay State Road, Boston.

MICHIGAN

National Survey of Families.—Future growth of American families will be studied by the University of Michigan Survey Research Center in 3,800 interviews across the U. S. during May, June, and July. The second in a series of studies sponsored by the Scripps Foundation for Research in Population Problems, the study is supported by a grant from the Rockefeller Foundation. The interviews are expected to provide "better understanding of certain problems concerning maternal health, family planning, and child bearing." Information gained from the interviews will help make forecasts of population trends. Wives selected for interviews represent a "carefully chosen sample" of married women in their child-bearing years. Each will receive an introductory letter from the Survey Research Center prior to the interviews, which will be conducted in the cities of Baltimore, Boston, Chicago, Cleveland, Detroit, Los Angeles, New York, Philadelphia, Pittsburgh, San Francisco, St. Louis, and Washington and their suburbs. Other cities and rural areas covered are scattered through the United States.

MISSOURI

Student Wins Medical History Contest.—Warren A. Heffron, Marshall, a second-year student in the University of Missouri School of Medicine, on May 6 was presented the first annual prize in the recently-established Arthur Rochford McComas Medical History Essay Contest for students in the School of Medicine. The title of Mr. Heffron's essay was "Dr. Sappington's Anti-Fever Pills" and related to Dr. John Sappington, an Arrow Rock physician of the mid-nineteenth century who was among the first to use quinine. The award, which carries a prize of $100, was presented to Mr. Heffron by Dr. Vernon E. Wilson, dean of the school, at a dinner in Memorial Student Union. Dr. McComas, who died in 1956, was an alumnus of the university and practiced in Sturgeon for more than 50 years. He was president of the Missouri State Medical Association in 1922-1923.

NEW MEXICO

Plan New Two-Year Medical School.—A $1,082,300 grant from the W. K. Kellogg Foundation to the University of New Mexico will assist the university over a five-year period to establish a school of the basic medical sciences which will encompass the first two years of the medical curriculum and then transfer the students to traditional four-year medical schools for their junior and senior years. In addition to serving the State of New Mexico, the new school of the basic medical sciences will be regional in character and reportedly should attract students from many of the West's 13 states, 8 of which do not have a medical school. A joint committee from the American Medical Association and the Association of American Medical Colleges will counsel the university in this pilot venture anticipated to provide an economical and practical method of increasing the supply of physicians. Further to develop this new two-year idea, the foundation will aid the establishment of at least one additional school of the basic medical sciences at a location yet to be announced. More than half of the initial grant will be used toward the planning phases of the new venture and the first five years of the school's operational budget including the salaries of administrative and instructional personnel. The remainder will be allocated toward the construction of a medical school facility on the Albuquerque campus, with the university financing the other two-thirds of such building cost. The new school at Albuquerque will be located in a metropolitan area of 235,000 inhabitants, having within its environs 14 licensed hospitals.

NORTH CAROLINA

University Appointments.—Dr. Harold D. Green was named Gordon Gray Professor of Physiology and Norman M. Sulkin, Ph.D., the William Neal Reynolds Professor of Anatomy at the Bowman Gray School of Medicine, Winston-Salem. Their appointments fill two of three named professorships in basic medical sciences. The professorships were recently established through a $500,000 grant from Mrs. Anne Reynolds Tate, of Pinehurst, and Mrs. Nathalie Gray Bernard, of Winston-Salem. A third professorship, the Odus M. Mull Professorship of Biochemistry, is expected to be filled in the near future. Dr. Green, prior to joining the faculty of Bowman Gray, served as instructor in physiology at the Western Reserve University School of Medicine and Yale University Medical School. A former president of the North Carolina Heart Association, he is a member of the editorial board of *Annual Review of Physiology, American Journal of Physiology,* and the *Journal of Applied Physiology.* Dr. Sulkin joined the Bowman Gray faculty in 1952 as an associate professor of anatomy. He is chairman of the section on biological sciences of the Gerontological Society and is a member of the editorial board of the *Journal of Gerontology* and *Gerontological Newsletter.*

PUERTO RICO

Report on Poliomyelitis.—The weekly report, "Morbidity and Mortality," of the Public Health Service for May 13 stated that 14 cases of paralytic poliomyelitis were reported in Puerto Rico for the week ended May 7. These were scattered in eight communities with five cases being reported in San Juan. A late report for the week ended April 30 included 12 paralytic cases—5 in Rio Piedras, near San Juan, and the rest scattered. The cumulative total number of paralytic cases in Puerto Rico is now 92.

TEXAS

Dr. Blocker Named Department Chairman.—Dr. Truman G. Blocker Jr. will become chairman of the department of surgery of the University of Texas Medical Branch, Galveston, effective July 1, succeeding Dr. Robert M. Moore, who has expressed a desire to reduce his administrative responsibilities. Dr. Blocker will be the fourth man to occupy the position in the 70-year-old history of the Medical Branch. The first was Dr. James E. Thompson, one of the team of English doctors who came to Galveston to help organize the original faculty in 1891. He was succeeded by the late Dr. Albert O. Singleton, who held the post from 1926 until his death in 1946. Dr. Blocker has been chief of the Medical Branch's division of Plastic and Maxillofacial Surgery since 1945 following 10 years of assistant and associate professorships in general surgery under Dr. Singleton. He is a governor of the American College of Surgeons and chairman of the American Board of Plastic Surgery and of the Public Health Surgery Study Section. Dr. Moore, who will continue to serve as an active, full professor in the department of surgery, is a representative of the Council on Medical Education and Hospitals of the American Medical Association, on the Conference Committee on Graduate Training in Surgery, and has served six years on the American Board of Surgery.

Medical Writing Fellowship Honors Late Editor.—The Texas Medical Association announced that Harriet Cunningham, managing editor of the *Texas State Journal of Medicine* and a member of the staff of the Texas Medical Association since 1945, passed away on Sunday, May 8. As a tribute, friends and associates are establishing the Harriet Cunningham Memorial Graduate Fellowship in Medical Writing at the University of Texas. A graduate fellowship in journalism for a student interested in medical writing, it will provide an opportunity for a "young person of exceptional ability to gain a background for medical writing and to secure some experience in this field as a part of the educational program." The student who is admitted into the University of Texas Graduate School to work toward a master's degree in journalism is required to take 30 semester hours of courses. He may enroll in a research or work-project conference course, engaging in a project which would be planned in cooperation with the Texas Medical Association. For the work on his thesis (six hours credit), the recipient of the fellowship would be expected to select a research area connected with medical writing. Requirements for holder of the Graduate Fellowship would be agreed upon through conference between representatives of the Texas Medical Association and the Scholarship Committee of the University of Texas School of Journalism. Preference likely would be given to candidates with one or more years of professional journalism experience, or to students who have demonstrated proficiency in science or science writing. The fellowship will be administered by the board of trustees of that association. For information, write the Texas Medical Association, 1801 N. Lamar Blvd., Austin, Texas.

WEST VIRGINIA

Survey of Medical Facilities.—The West Virginia State Medical Association's Rural Health Committee has authorized the chairman, Dr. Earl L. Fisher, of Gassaway, to conduct a statewide survey concerning medical, hospital, and nursing facilities available in the various towns over the state with a population of 700 or over. Dr. Fisher asked the secretaries of the numerous Lions Clubs over the state to assist in the survey. The State Medical Association annually awards a scholarship to a member of the freshman class of the School of Medicine of West Virginia University. The selection is made by the Association's Committee on Medical Education and Scholarships, and the recipient agrees, upon the completion of his four years in medical school and internship, to practice for four years in a Rural Community selected by the committee after consultation with the Committee on Rural Health. The information obtained by the Rural Health Committee as the result of questionnaires returned by secretaries of Lions Clubs will at the proper time be made available to the Committee on Medical Education and Scholarships.

Society News.—Dr. John A. B. Holt, of Charleston, was elevated to the presidency of the West Virginia Academy of Ophthalmology and Otolaryngology during the 13th annual meeting of that organization April 10-12. Dr. Holt succeeds Dr. Nime K. Joseph, of Wheeling, the retiring president. Other new officers elected are as follows: Dr. Albert C. Esposito, Huntington, president-elect; Dr. William K. Marple, Huntington, vice-president; Dr. Worthy W. McKinney, Beckley, secretary-treasurer; and Dr. R. Alan Fawcett, Wheeling, director (two-year term).——At the annual meeting of the West Virginia Chapter, American College of Surgeons, April 1-2, Dr. Ray E. Burger, of Welch, was installed as president for the coming year. He succeeds Dr. Kenneth G. MacDonald, of Charleston. Dr. Victor S. Skaff, Charleston, was elected vice-president, and Dr. Jack C. Morgan, Fairmont, was named secretary-treasurer. Elected as councillors were Drs. John O. Rankin and Charles D. Hershey, of Wheeling, and Kenneth G. MacDonald and William D. McClung, of Charleston.

GENERAL

Annual Golf Tournament.—The 44th annual tournament of the American Medical Golf Association will be held at the Diplomat Country Club, Hollywood-by-the-Sea, Fla., on Monday, June 13. The fee of $25 includes greens fees, luncheon, cocktails, and dinner. USGA rules will govern all play. For registration and information, write Dr. C. Howard McDevitt Jr., 320 Alhambra Circle, Coral Gables, Fla. Dr. John A. Growdon, Kansas City, Mo., is president of the association.

Postconvention Meeting in Bahamas.—A postconvention meeting in Nassau will be conducted by Bahamas Conferences June 18-25 following the A.M.A. meeting in Miami Beach. Papers will be presented each morning from 9:30 a. m. to noon and in the evening from 6 to 7 p. m. The Emerald Beach Hotel is the headquarters for this conference. The registration fee is $15. For information, write Mr. Irvin M. Wechsler, Executive Director, Bahamas Conferences, P. O. Box 1454, Nassau, Bahamas.

Surgeons Visit Russia.—The Ministry of Health of the Russian government invited three U. S. surgeons to Moscow as guests of the U. S. S. R. to participate in the 27th Congress of Surgeons of the U. S. S. R. Dr. Henry Swan II, head, department of surgery, University of Colorado School of Medicine, Denver, Dr. Waltman Walters, senior surgeon, Mayo Clinic, Rochester, Minn., and Dr. Isidor S. Ravdin, vice-chancellor, University of Pennsylvania, were guests at the congress. This was reported to be the first time the Russians had invited a group of U. S. surgeons to one of their meetings.

Editorial Appointments for World Journal.—The headquarters secretariat of the World Medical Association announced the appointment of Dr. J. Gosset, editor of *Concours Medical*, of Paris, France, to the position of associate editor of *World Medical Journal*, official publication of the association. Dr. Stanley S. B. Gilder, formerly editor of the *Journal of the Canadian Medical Association* is the executive editor of *World Medical Journal*. The members of the editorial board include the executive and associate editor, the business manager, and three members of council, namely: Dr. A. Fernandez Conde (Cuba); Dr. Hugh Clegg (United Kingdom); and Dr. M. Poumailloux (France).

Convention of Biological Psychiatry.—Twenty-five formal papers are scheduled to be presented at the 15th annual convention of the Society of Biological

Psychiatry, June 10-12, at the Deauville Hotel, Miami Beach, Fla. A symposium on methodology in treatment is planned for the afternoon of June 11. The Academic Lecture, "The Role of Biological Treatment in Comprehensive Psychiatric Management," will be given by Dr. Hans Hoff, Vienna, Austria, the morning of June 12, and the presidential address will be given by Dr. Paul H. Hoch, New York City, that afternoon. For information, write Dr. George N. Thompson, 2010 Wilshire Blvd., Los Angeles 57, Secretary-Treasurer.

Annual Meeting of Medical Women.—The 1960 annual meeting of the American Medical Women's Association will be held June 9-12 at the Carillon Hotel, Miami Beach, Fla., under the presidency of Dr. Jessie Laird Brodie, Portland, Ore. Dr. Leonard W. Larson, Bismarck, N. D., Chairman, Board of Trustees, American Medical Association, will be the featured speaker at the dinner June 10, 8:30 p. m. A debate, "Should the Older Person Live with His Children?," will be held the afternoon of June 11. That evening at the inaugural banquet, Dr. Claire F. Ryder, Alexandria, Va., will present "A Modern Day Challenge—Disability" as the inaugural address. On June 12, a panel discussion, "Prevention and Control of Disability," is scheduled. For information, write Miss Lillian T. Majally, 1790 Broadway, New York 19, Executive Secretary.

Meeting on Investigative Dermatology.—The 21st annual meeting of the Society for Investigative Dermatology, Inc., will be held June 13-15 at the Hotel Delido, Miami Beach, Fla. Dr. Thomas B. Fitzpatrick, Boston, will present "Clinical and Biochemical Studies of Human Albinism" as the presidential address to open the scientific session. Papers which include Canadian authors are "The Capillary Responses in Psoriatic Skin," Drs. Paul Telner and Zoltan Fekete, Montreal, and "Studies in Vascular Permeability of the Human Skin Using Coomassie Blue as Indicator," Dr. Frederick G. Kalz and Dr. Fekete, Montreal. The program includes a total of 35 papers. A dinner is planned for 7 p. m., June 13. For information, write Dr. Herman Beerman, 255 S. 17th St., Philadelphia 3, Secretary-Treasurer.

Meeting of Therapeutic Society.—The American Therapeutic Society will hold its 61st annual meeting June 9-12 in Miami Beach, Fla., with headquarters at the Barcelona Hotel. The president of the society, Dr. Charles L. Leedham, Cleveland, will serve as chairman of the opening session. The lecture for the sixth Oscar B. Hunter Memorial Award in Therapeutics, "Paradoxical Renal Hemodynamic Responses to Blood Pressure Reduction Comparing Acute and Long Term Observations," will be given by Dr. John H. Moyer, chairman, department of internal medicine, Hahnemann Medical College and Hospital, Philadelphia. The ninth annual Lewis Harvie Taylor Lectureship will be given by Dr. Hugh R. Butt, Rochester, Minn., titled "Changing Concepts of Bilirubin Metabolism." A total of 44 papers will be presented. For information, write Dr. Oscar B. Hunter Jr., 915-19th St., N. W., Washington, D. C., Secretary.

High Incidence of Respiratory Diseases.—In 1959, for the third successive year, diseases of the respiratory system ranked first among the causes of disability lasting eight days or more among employees of the Metropolitan Life Insurance Company, it is reported by the company's statisticians. The incidence rate of such diasability—157 per 1,000 personnel—was about the same as in 1958, but somewhat lower than that for 1957. The relatively high incidence of disability in the past three years is ascribed to the widespread prevalence of influenza in the late months of 1957 and in the early months of 1958 and 1959. Disability rates were more than 1½ times as high for women as for men under age 25, about three times as high at ages 25-44, and slightly over twice as high at ages 45 and over. Diseases of the digestive system ranked second to respiratory disease as a cause of disability in both men and women. Accidental injuries ranked third among women and fourth among men. Diseases of the circulatory system—including heart disease—ranked third among men, but well down the list for women.

Meeting of Diabetes Group.—The American Diabetes Association, Inc., will meet at the Deauville Hotel, Miami Beach, Fla., June 11-12. Thirty-nine papers are scheduled for presentation. The Banting Memorial Lecture, "Childhood Diabetes—Its Course, and Influence upon the Second and Third Generations," will be given at the opening scientific session the morning of June 11 by Dr. Priscilla White, assistant professor of pediatrics, Tufts University Medical School, Boston. At the banquet that evening, Dr. Francis D. W. Lukens, Philadelphia, president of the association, will present an address, after which the Lilly Award will be presented to Dr. Albert E. Renold, assistant professor of medicine, Harvard Medical School, Boston; Banting medals will be received by Dr. White and Dr. J. B. Collip, dean of medicine, Faculty of Medicine, University of Western Ontario, London, Ont., Canada; and a citation will be awarded to Miss Edith Jenkins, of the Indianapolis Diabetes Association. Discussions will follow the formal presentations of papers. For information, write Mr. J. Richard Connelly, 1 E. 45th St., New York 17, Executive Director.

Cardiovascular Meeting in Miami Beach.—The International Cardiovascular Society, North American Chapter, will hold its eighth scientific meeting

June 11 at the DeLido Hotel, Miami Beach, Fla. Dr. Henry Haimovici, of New York City, will preside over the opening session and will present the presidential address at the afternoon session. The guest lecturer at the meeting will be Dr. W. Stanley Hartroft, Mallinckrodt Professor and chairman, department of pathology, Washington University School of Medicine, St. Louis. A total of 18 papers are scheduled for presentation. The informal dinner will be followed by a plethysmographic conference which will include the following papers:

Applications of Rheoplethysmography, Dr. George E. Burch, New Orleans.
Clinical Plethysmography in Specific Vascular Diseases, Dr. Robert J. H. Goetz, New York City.
Arteriosclerosis Obliterans of the Upper Extremities: A Plethysmographic Appraisal, Dr. Haimovici and Enrique Spiegler, New York City.
Plethysmographic Observations in Systemic Disease State, Dr. David I. Abramson, Chicago.
Application of Plethysmography to the Study of Veins in Health and Disease, Dr. Travis Winsor, Los Angeles.

For information write Dr. Paul T. DeCamp, 3503 Prytania St., New Orleans 15, Secretary.

Shift Dates for Conference on Physicians and Schools.—The time and place of the 1961 National Conference on Physicians and Schools will be shifted from its customary October date in suburban Highland Park (Ill.) to March 9-11 in Chicago. The new locale of the conference will be the Sheraton Towers Hotel on North Michigan Avenue. The eighth national conference was advanced to this date so that it could follow immediately after the half-century birthday celebration of the Joint Committee on Health Problems in Education of the National Education Association and the American Medical Association, Wednesday, March 8. The new location provides hotel meeting facilities convenient to the headquarters office of the A. M. A. at 535 N. Dearborn St. The general objectives of the conference—to foster interprofessional agreement on ways and means to improve health and fitness programs for school-age youth—will remain the same. Representatives of state departments of health, state departments of education, and state medical societies will be invited to send delegates to the conference. Additional representation will be drawn from national voluntary agencies with a major interest in health problems of school-age children. Leaders in the school health field, from medicine, education, and public health, will serve as consultants.

Physician and Student Share Exhibit Honors.—Dr. Robert C. Reeder, a resident at St. Francis Memorial Hospital in San Francisco, and Rod C. Perkins, a junior medical student at Indiana University, shared top honors as scientific exhibitors at the 10th annual meeting of the Student American Medical Association. Dr. Reeder and Mr. Perkins were named winners of the first place prizes in the third annual competition for the SAMA–Lakeside Awards. Each received a $500 prize and an expense-free trip to the American Medical Association convention in Miami Beach, where they will display their exhibits again. Dr. Reeder's prize winning scientific exhibit is titled "Fractures of the Facial Skeleton." Mr. Perkins' exhibit is titled "Disk Oxygen-Thermal Exchanger." The SAMA–Lakeside Awards are designed to encourage a greater use of scientific exhibits as a medium of professional communication. Second place winners of the 1960 award are Dr. Richard F. McLauchlin Jr., a resident at St. Mary's Hospital, San Francisco, for the exhibit "A Study of the Subgross Pulmonary Anatomy in Various Mammals and Man" and Mr. Robert W. Begley, a medical student at Indiana University, for "Neuropharmacology of the Gamma Loop." Second place consists of an award certificate and $250. Third place winners are Dr. Arnold K. Brenman, a resident at Temple University School of Medicine, for the exhibit "Photography in Otologic Microsurgery" and Mr. Charles F. Johnson, a medical student at the University of California School of Medicine at Los Angeles, for "Tumors of Viral Etiology." Third place prize consists of an award certificate and $100.

New Society for Nutrition Formed.—The formation of the American Society for Clinical Nutrition was announced during the meetings of the American Society for Clinical Investigation and the American Federation for Clinical Research May 1. Arrangements are being made to affiliate the ASCN with the American Institute for Nutrition. Dr. Richard W. Vilter, chairman, department of medicine, University of Cincinnati College of Medicine, was elected president of the ASCN by the charter members at the organization's first meeting. Other officers of the new society include president-elect, Dr. Robert E. Olson, head, department of biochemistry and nutrition, University of Pittsburgh Graduate School of Public Health, and secretary-treasurer, Dr. Robert E. Hodges, associate professor of medicine, University of Iowa School of Medicine, Iowa City. A four-point list of objectives adopted at the first meeting states that the ASCN shall:

1. Foster high standards for research on human nutrition.
2. Promote undergraduate and graduate education in human nutrition.
3. Provide a place and opportunity for research workers in problems of human nutrition to present and discuss their research activities and results.
4. Provide a journal for the publication of meritorious work on human nutrition.

The new society has been incorporated under the laws of the state of New York, and will have its headquarters at the office of the secretary-treasurer.

It voted to hold its first annual meeting in 1961 in conjunction with those of the American Society for Clinical Investigation and the American Federation for Clinical Research. The organizing group plans to adopt *The American Journal of Clinical Nutrition* as its official publication. Membership in the ASCN is by nomination and will include physicians and other biological scientists actively engaged in research and teaching in the areas of human nutrition and metabolism.

Medical Examiners for Pilot Applicants.—Effective June 15, the Federal Aviation Agency will require all applicants for a student or private pilot (Class 3) medical certificate to take their medical examinations solely from designated aviation medical examiners. The regulations currently require applicants for Airline Transport Pilot (Class 1) and Commercial Pilot (Class 2) medical certificates to be examined by designated medical examiners. The change reestablishes the previous practice which required applicants for all three classes of airman medical certificates to take their medical examinations only from designated medical examiners. Before adopting the change, FAA provided information about the proposal to interested parties for comment and held a public hearing. The American Medical Association, Aerospace Medical Association, the Flying Physicians Association, the Civil Aviation Medical Association, and a majority of individual doctors who commented, supported the proposal. Opposition was registered by the Aircraft Owners and Pilots Association, other groups, some physicians and private individuals. An agency survey showed that of the airmen examined by nondesignated examiners, 84% of those who did not meet the standards were nevertheless given certificates by the examining physicians.

FAA now has about 2,000 designated medical examiners and over 25% of the 240,000 Class 3 pilots currently select doctors from this group when seeking their medical examinations. The Civil Air Surgeon announced that he will welcome an application for designation from any physician who wishes to join in the agency's efforts in support of air safety. Designated examiners will have responsibility for maintaining detailed knowledge of a manual of instruction, published standards, and periodic directives issued by the agency. In addition, they must possess the equipment and facilities necessary to carry out the prescribed examinations. Airmen holding Class 3 medical certificates are required to be examined every two years. For information, write the Federal Aviation Agency, Washington, D. C.

Program for Students to Study Abroad.—A fellowship program designed to further medical education by sending future physicians to remote areas of the world was announced by the Association of American Medical Colleges. The three-year program, established under a $180,000 grant from Smith Kline & French Laboratories, is open to all medical students who have completed their third year of study. Scheduled to begin this summer, the program will permit an average of 30 students to participate each year. Eligible students prepared to spend an average of 12 weeks working in foreign locales are urged to submit applications to their respective deans for review. Following initial screening, up to three applications from each school will be forwarded to a panel of physicians who will make up the selection committee for the SK&F foreign fellowships. Awards will be made on the basis of the applicant's ability and objectives with special consideration given to those programs which cannot be realized in the United States and through which the student can bring back "valuable knowledge" to this country. The cash award for the fellowship will be made on an individual basis. In some cases, a contribution will be made for the student's spouse if this seems desirable in terms of the objectives of the trip. After completion of the fellowship, each student will be required to submit a written report on his experiences to the selection committee. Applications by the students must contain a letter detailing the proposed trip as well as a complete estimate of the expenses to be incurred and the total amount of the fellowship requested. The letter must include the location to be visited, purpose of the trip, personal reasons for wishing to undertake the program, and the amount of time that will be involved. All other pertinent data that will aid the deans and selection committee also should be included. In addition, a personal history of the applicant and a letter of acceptance from the foreign sponsor with whom the student will work abroad also are required.

CANADA

Meeting of Biological Societies.—The third annual meeting of the Canadian Federation of Biological Societies will be held June 8-10 at the University of Manitoba, Winnipeg. Special council meetings will precede the formal discussions June 6 and 7. The program is divided under the following section headings: Blood, Cancer, Kidney and Electrolytes, Neurochemistry, Biochemistry, Endocrinology, Nutrition, Pharmacology, Biochemistry and Physiology, Circulation and Respiration, Nervous System and Muscle, Catecholamines, Enzymes, Histology and Embryology, Mast Cells. The annual federation dinner will be held the evening of June 9. A program of exhibits is planned. For information, write Dr. Edward H. Bensley, Montreal General Hospital, 1650 Cedar Ave., Montreal 25, P.Q., Honorary Secretary.

FOREIGN

New Journal of Gastroenterology.—The British Society of Gastroenterology and the British Medical Association are joining forces to produce the new quarterly journal, *GUT*. The object of *GUT* is to publish original papers and reviews concerned with practice and research in gastroenterology, including alimentary, hepatic, or pancreatic disease, and papers may cover the medical, surgical, radiological, or historical aspects. They may also deal with the basic sciences concerned with the alimentary tract, including experimental work. Reports of single cases which are of interest in relation to a wider field of research will be published from time to time. A section will be devoted to short papers on laboratory and surgical techniques and methods of investigation where these are not part of a larger survey. The first issue will contain about 86 pages of text, quarto in format, and will be illustrated. The journal will appear in March, June, September, and December of every year. Postpaid price is $10, U. S. and Canada. For information, write British Medical Association Publications, Medical Market Research, Inc., East Washington Square, Philadelphia 5.

CORRECTION

Date of Death for Dr. Grubbe.—On page 193 of the May 14 issue of The Journal, the last line of the obituary on Dr. Emil Herman Grubbe, giving the date of Dr. Grubbe's death, should have read "March 26, aged 85, of cancer of the lungs."

EXAMINATIONS AND LICENSURE

MEDICAL SPECIALTY BOARDS

American Board of Anesthesiology: *Written.* Various locations, June 24. Final date for filing application was January 10. Sec., Dr. Forrest E. Leffingwell, 217 Farmington Ave., Hartford 5, Conn.

American Board of Dermatology: Final date for filing applications of candidates completing training by October 15, 1960 is March 1, 1961. *Written.* Several cities, June 5, 1961. *Oral.* Philadelphia, Oct. 13-16, 1961. Sec., Dr. Maurice J. Costello, One Haven Avenue, New York 32, New York.

American Board of Internal Medicine: New York City, Nov. 14-17. Closing date for filing application is July 1. *Written.* Oct. 17. Closing date for filing application was May 1. Schedule for 1961. *Written Examination*, October 16. *Oral Examinations.* New Orleans, Jan. 30-Feb. 2; Chicago, April 4-7; Los Angeles, Sept. 26-29; New York City, Nov. 7-10. Closing date for acceptance of applications for the January and April examinations is October 1, 1960, and for the September and November examinations is June 1, 1961. Sec.-Treas., Dr. William A. Werrell, One West Main St., Madison 3, Wis.

American Board of Neurological Surgery: Examination given twice annually, in the spring and fall. In order to be eligible a candidate must have his application filed at least six months before the examination time. *Oral.* New Haven, Nov. 6-9. Sec., Dr. Donald D. Matson, 300 Longwood Ave., Boston, Mass.

American Board of Obstetrics and Gynecology: Applications for certification in Part I, new and reopened, are now being accepted. Deadline for receipt of applications is August 1, 1960. *Oral Examination, Part II.* Chicago, April 7-14, 1961. Final date for filing application is August 1, 1960. After July 1, 1962, a minimum of three years of approved progressive residency training will be required. Training by preceptorship will no longer be acceptable. The initiation of preceptorships will not be approved after July 1, 1960. Sec., Dr. Robert L. Faulkner, 2105 Adelbert Road, Cleveland 6.

American Board of Ophthalmology: *Written.* Jan. 23, 1961. Deadline for filing applications is July 1. *Oral.* Chicago, Oct. 3-7. Sec., Dr. Merrill J. King, Box 236 Cape Cottage Branch, Portland, Maine.

American Board of Orthopaedic Surgery: *Oral and Written, Part II.* Miami Beach, Jan. 3-5, 1961. Final date for filing application is July 1. Sec., Dr. Sam W. Banks, 116 South Michigan Ave., Chicago 3.

American Board of Otolaryngology: *Oral.* Chicago, Oct. 3-6. Final date for filing application was April 1. Sec., Dr. Dean M. Lierle, University Hospitals, Iowa City.

American Board of Pediatrics: *Written.* New York City, January 1961. Final date for filing application is Dec. 1. Administrative Sec., Mrs. Eleanor J. Mitchell, Rosemont, Pa.

American Board of Physical Medicine and Rehabilitation: *Oral and Written.* New York, June 17-18. Sec., Dr. Earl C. Elkins, Mayo Clinic, Rochester, Minn.

American Board of Proctology: *Oral and Written, Parts I and III.* Philadelphia, Sept. 24. Final date for filing application is June 30. Sec., Dr. Stuart T. Ross, 520 Franklin Ave., Garden City, N. Y.

American Board of Psychiatry and Neurology: New York, New York, Dec. 12-13, New Orleans, Mar. 20-21, 1961. Sec., David A. Boyd, Jr., 102-110 Second Ave., S.W., Rochester, Minn.

American Board of Radiology: *Examination.* Cincinnati, June 6-10; Dec. 10-13. Deadline for filing applications for the June examination was Jan. 1. Filing deadline for the December examination is July 1. A special examination in Nuclear Medicine (for those diplomates in Radiology or Therapeutic Radiology) will be offered provided there are sufficient applications. Sec., Dr. H. Dabney Kerr, Kahler Hotel Bldg., Rochester, Minn.

American Board of Surgery: *Written.* (Part 1), Various Centers, Dec. 7. *Candidates are urged to apply several months before completion of training requirements.* The closing date for filing applications is August 1. Those completing training requirements after September 30 cannot be considered for the December Part I examination of the same year. *Oral.* (Part II)—New Haven, Sept. 26-27; Indianapolis, Oct. 24-25; Buffalo, Nov. 14-16; Nashville, Dec. 12-13; Philadelphia, Jan. 16-17; Houston, Feb. 13-14; Columbus, Ohio, Mar. 13-14; New York City, April 19-20; Portland, Ore., May 15-16; San Francisco, May 18-19. No examinations will be held in June, July or August. Sec.-Treas., Dr. John B. Flick, 1617 Pennsylvania Blvd., Philadelphia 3.

Board of Thoracic Surgery: *Written.* Various centers throughout the country, Sept. 9. Final date for filing application is July 1. *Oral.* Oct. 1960. Final date for filing application is July 1. Sec., Dr. Wm. M. Tuttle, 1151 Taylor Ave., Detroit 2.

American Board of Urology: *Written.* December. *Oral-Clinical.* Chicago, February 1961. Exec. Sec., Mrs. Ruby L. Griggs, 30 Westwood Road, Minneapolis 26.

GOVERNMENT SERVICES

VETERANS ADMINISTRATION

Data Processing.—A data processing staff was established in the department of medicine and surgery, Washington, D. C. The director of the staff is Dr. Milton I. Schwalbe, who was transferred from the position of director of professional services of the Manhattan VA hospital in New York City. The staff, directly responsible to the VA chief medical director, will plan, develop, and coordinate integrated automatic data processing applications involving administrative activities for the department of medicine and surgery and on a nationwide basis. The VA chief medical director, Dr. William S. Middleton, believes there is a high potential for application of automatic data processing to medical research and clinical evaluation.

Personal.—Dr. Oreon K. Timm, area medical director for the Veterans Administration in St. Paul, Minn., since January, 1958, was appointed deputy to the VA assistant chief medical director for operations in Washington, D. C. Dr. Timm will assist in directing operations of the VA's 170 hospitals, 91 outpatient clinics, and 18 domiciliary homes. He succeeds Dr. Horace B. Cupp, who is retiring after 30 years of VA medical service.—Dr. Charles P. Henke, formerly manager of the Veterans Administration's general medical and surgical hospital in Pittsburgh, was named director of domiciliary facilities for the VA with headquarters in Washington, D. C. In his new position, Dr. Henke directs the operations of the VA's 18 domiciliary homes. He succeeds Dr. M. H. Travers, who retired from government service.

PUBLIC HEALTH SERVICE

Radiation Health Data.—A new monthly technical publication, *Radiation Health Data*, gives levels of radioactivity in air, water, and milk. Among the contents of the first issue are data on radioactive strontium (Sr^{90}) in milk collected during November, 1959, at 12 locations in the United States by the Public Health Service; milk collected during the same month at 3 locations by the Atomic Energy Commission; and monthly milk collections for the year ended August, 1959, at 6 locations in Minnesota as reported by the health department of that state.

Radioactivity in air samples collected at 44 points in the United States during November, 1959, by the Public Health Service and at 12 Latin American and 6 United States points along the 80th meridian (west), also for November, 1959, by the U. S. Naval Research Laboratory in cooperation with the Atomic Energy Commission is also reported. Radioactivity in surface water samples collected during October, 1959, by the Public Health Service at 61 points throughout the United States and Sr^{90} levels in New York City tap water for September, 1959, are among the other tabulations.

Most of the radiation measurements that will be carried by the new publication will be in the form of raw data which are not immediately susceptible to meaningful analyses or interpretation, but as these data accumulate and as more knowledge of the biological effects of radiation begins to come out of laboratory, clinical, and epidemiologic research by federal, state, and local agencies, by universities, and by industry, such analyses and interpretations will become more feasible. The price of the publication is 50 cents per single issue and $3.00 for a six-month subscription, from the Office of Technical Services, U. S. Department of Commerce, Washington 25, D. C.

Personal.—Dr. Robert L. Zobel was appointed medical officer in charge of the Indian Health Area office at Albuquerque, N. Mex., effective July 1. He succeeds Dr. Charles R. Mallary, recently named deputy chief of the Public Health Service's bureau of medical services. Dr. Zobel will administer health and medical care services provided by the Public Health Service for about 100,000 Indians on all federal Indian reservations in New Mexico and Colorado, and on the Navajo reservation in Arizona and Utah. Since 1958, he has directed Indian health services in Idaho, Oregon, Washington, Montana, and Wyoming.

SELECTIVE SERVICE SYSTEM

Doctor Draft.—The Armed Forces continue to require the services of most physicians liable for military service under the Universal Military Training and Service Act. All reserve officers deferred for residency in most specialties will be called. Shortages exist and will continue in certain specialties and in the group of officers who have not specialized. The Department of Defense has found it unnecessary to requisition physicians through the Selective Service System since early in 1957. This has been so only because sufficient numbers of physicians sought reserve commissions and thus made themselves available for the call to active duty. There is a continuing need for applications for the residency program, as well as for reserve commissions and active duty at the conclusion of internship.

DEATHS

Ciancimino, Charles Joseph Ⓜ Brooklyn; University and Bellevue Hospital Medical College, New York City, 1924; fellow of the International College of Surgeons; member of the board of governors and treasurer of the Kings County Physicians Guild; member of the medical board and attending surgeon at the St. John's Long Island City Hospital in Long Island City; associate surgeon at Kings County Hospital; died Feb. 17, aged 60, of coronary thrombosis.

Clinton, James Francis Ⓜ Menlo Park, N. J.; Hahnemann Medical College and Hospital of Philadelphia, 1939; interned at the Bridgeport (Conn.) Hospital; served a residency at the New Jersey State Hospital in Marlboro, where he was acting clinical director 1954-1955; staff officer of the U. S. Coast Guard 1948-1949; member of the American Psychiatric Association; associated with the New Jersey State Diagnostic Center; from 1941 to 1948 associated with the E. I. Du Pont Company; died in New York City March 20, aged 44, of coronary thrombosis.

Cochran, Williams Ⓜ Auburndale, Mass.; Harvard Medical School, Boston, 1929; for many years served in North China as a medical missionary under the auspices of the Presbyterian Board of Missions; certified by the National Board of Medical Examiners; served on the faculty of his alma mater; on the staff of the Massachusetts General Hospital in Boston; died March 29, aged 56, of coronary disease.

Cohn, Edwin Arthur, Chicago; Illinois Medical College, Chicago, 1909; died March 20, aged 83, of cerebral thrombosis.

Cooper, Maurice D. Ⓜ Winnebago, Minn.; University of Minnesota College of Medicine and Surgery, Minneapolis, 1907; member of the American Academy of General Practice; on the staff of the Community Memorial Hospital; died in the Methodist Hospital, St. Louis Park, March 25, aged 78, of coronary occlusion.

Dinsmore, Andrew Jackson, Decatur, Ala.; Chicago College of Medicine and Surgery, 1916; veteran of World War I; on the staff of Decatur General Hospital; died March 19, aged 70, of myocardial infarction.

Donahue, Matthew Thomas Ⓜ Cleveland; University of Cincinnati College of Medicine, 1920; died in the Evangelical Deaconess Hospital March 12, aged 63.

Dutton, Harry Horace, Tacoma, Wash.; University of Vermont College of Medicine, Burlington, 1914; specialist certified by the American Board of Psychiatry and Neurology; veteran of World War I; served as superintendent of the Northern State Hospital in Sedro Woolley; at one time assistant superintendent of the Western State Hospital in Fort Steilacoom; died in the Tacoma General Hospital March 20, aged 70, of myocardial infarction and coronary thrombosis.

Economou, Michael G., Canton, Ohio; National University of Athens School of Medicine, Greece, 1899; died in the Mercy Hospital March 11, aged 83, of cerebral hemorrhage, monocytic leukemia, and arteriosclerotic heart disease.

Ellis, Melvin, Sacramento, Calif.; University of Southern California Medical Department, Los Angeles, 1909; died in St. Vincent's Hospital March 31, aged 78, of multiple pulmonary emboli.

Elsey, James Ralph, Glenwood, Minn.; Washington University School of Medicine, St. Louis, 1898; veteran of World War I; formerly mayor; served on the staff of the Glenwood Community Hospital, where he died March 20, aged 88.

Fentin, Edward, Quincy, Mass.; Middlesex University School of Medicine, Waltham, 1932; died in the New England Deaconess Hospital, Boston, Feb. 23, aged 51, of uremia due to lymphocytoma with renal involvement.

Filice, Francesco E., Long Branch, N. J.; Universita degli Studi di Roma. Facolta di Medicina e Chirurgia, Italy, 1905; died March 22, aged 82.

Flanders, John Aiken, Chicago; Loyola University School of Medicine, Chicago, 1917; died in the Chicago State Hospital March 29, aged 77, of arteriosclerotic cardiovascular disease.

Forman, Isador Ⓜ Philadelphia; Temple University School of Medicine, Philadelphia, 1926; specialist certified by the American Board of Obstetrics and Gynecology; clinical professor of obstetrics and gynecology at his alma mater; on the staff of the Philadelphia General Hospital; died April 10, aged 57, of myocardial infarction.

Friedman, Joseph, Brooklyn; Long Island College Hospital, Brooklyn, 1906; served on the staff of the Beth Moses Hospital; died April 4, aged 75, of acute myocardial infarction.

Ⓜ Indicates Member of the American Medical Association.

Friesch, Wenzel, Denver; University of Colorado School of Medicine, Denver, 1927; member of the Industrial Medical Association; a member of the staff at St. Luke's Hospital, where he died April 2, aged 59, of chronic glomerulonephritis.

Fullilove, Robert Elliott Sr., Yazoo City, Miss.; Meharry Medical College, Nashville, Tenn., 1907; died March 17, aged 83.

Glosser, Herbert Hartman, Wellsville, N. Y.; University of Pennsylvania Department of Medicine, Philadelphia, 1899; specialist certified by the American Board of Ophthalmology; member of the American Academy of Ophthalmology and Otolaryngology; formerly practiced in Buffalo, N. Y.; died March 11, aged 83, of acute coronary disease.

Graham, Allison Tower Ⓢ Oklahoma City, Okla.; Memphis (Tenn.) Hospital Medical College, 1913; veteran of World War I; died in the Capitol Hill General Hospital March 28, aged 68, of gastric ulcer with hemorrhage.

Gutch, Thomas Ernst, Albia, Iowa; Barnes Medical College, St. Louis, 1898; fellow of the American College of Surgeons; served as health officer; associated with the Bituminous Casualty Corporation of Rock Island, Ill.; on the staff of the Mercy Hospital in Des Moines and the Monroe County Hospital; died March 18, aged 85.

Hall, Arche Carl, Detroit; College of Physicians and Surgeons, Baltimore, 1911; fellow of the American College of Surgeons; associated with the Harper Hospital; died in the Veterans Administration Hospital in Allen Park, Mich., March 30, aged 78, of pneumonia.

Handy, Stafford Odell Ⓢ Lynchburg, Va.; Medical College of Virginia, Richmond, 1928; specialist certified by the American Board of Radiology; past-president of the Lynchburg Academy of Medicine; associated with the Virginia Baptist, Marshall Lodge Memorial, and Lynchburg General hospitals; died in the Medical College of Virginia, Hospital Division, Richmond, March 26, aged 55, of burns received Feb. 18, when his bed caught fire.

Harned, Ezra Clayborne, Louisville, Ky.; University of Louisville Medical Department, 1892; died March 25, aged 91, of arteriosclerotic heart disease.

Hayward, George Earnest Ⓢ Meadville, Pa.; Hahnemann Medical College and Hospital of Philadelphia, 1910; past-president of the Crawford County Medical Society; for many years a member of the board of health of Meadville; served as chairman of the Meadville Civil Service Commission; formerly mayor; associated with the Meadville City Hospital, where he died March 22, aged 74, of cerebral hemorrhage.

Hendricks, Henning Vitalis, Kalkaska, Mich.; Harvard Medical School, Boston, 1909; died March 18, aged 78, of intestinal obstruction.

Herrin, Charles Edward Ⓢ Cullman, Ala.; Chattanooga (Tenn.) Medical College, 1902; specialist certified by the American Board of Otolaryngology; associated with the Cullman Hospital; died March 20, aged 84.

Hillas, William Joseph Ⓢ Tucson, Ariz.; Chattanooga (Tenn.) Medical College, 1910; veteran of World War I and was decorated by three kings for his work with the Red Cross European relief program after the war; for many years practiced in Chattanooga, Tenn.; died in St. Mary's Hospital March 26, aged 81, of congestive cardiac failure.

Hillman, C. Van Kirk Ⓢ Seattle; Northwestern University Medical School, Chicago, 1942; interned at the King County Hospital, where he served a residency; fellow of the American College of Surgeons; specialist certified by the American Board of Surgery; veteran of World War II; clinical associate in surgery and anatomy at the University of Washington School of Medicine; associated with the Swedish, Doctors, and Providence hospitals; on the courtesy staffs of the Maynard, Columbus, and Seattle General hospitals; died in the University of Washington Infirmary March 22, aged 43, of nephritis with hypertensive cardiovascular disease.

Howell, Donald MacLean Ⓢ Saginaw, Mich.; Detroit College of Medicine and Surgery, 1919; specialist certified by the American Board of Otolaryngology; member of the American Academy of Ophthalmology and Otolaryngology; fellow of the American College of Surgeons; died in the Ford Hospital, Detroit, April 2, aged 71.

Hudgel, Charles R., Boise, Idaho; Baltimore Medical College, 1893; died March 23, aged 90.

Hudson, Eugene Henry, Anderson, Ind.; Meharry Medical College, Nashville, Tenn., 1917; died in the Cleveland Clinic, Cleveland, March 21, aged 74, of carcinomatosis.

Jaffe, Jacob Karl Ⓢ Philadelphia; Medico-Chirurgical College of Philadelphia, 1905; formerly on the faculty of the University of Pennsylvania Graduate School of Medicine; served as medical director of the Workmen's Circle Home for the Aged in Media and the International Ladies Garment Workers Union Health Center; died in the Graduate Hospital of the University of Pennsylvania April 7, aged 78, of heart disease.

John, Baxter Schooley, Washington, D. C.; University of Maryland School of Medicine and College of Physicians and Surgeons, Baltimore, 1921; associated with the Doctors Hospital; died in Englewood, Fla., March 4, aged 66, of coronary occlusion.

Johnson, Lester Sheldon Ⓜ Chicago; Loyola University School of Medicine, Chicago, 1921; staff member of the Norwegian American Hospital; veteran of World War II; died in the Veterans Administration Hospital, Hines, Ill., April 3, aged 70, of cerebral hemorrhage.

Jordan, Stanley Youngs, Ames, Iowa; Washington University School of Medicine, St. Louis, 1948; interned at the Presbyterian Hospital in Chicago; served a residency in pathology at St. Louis County Hospital in Clayton, Mo., and a fellowship in internal medicine at the Mayo Foundation in Rochester, Minn.; staff physician at the Iowa State University health service; an officer in the medical corps of the U. S. Army Reserve from September, 1949, to September, 1951; died in the Iowa State College Hospital March 26, aged 35.

Kowalski, Joseph Vincent Ⓜ Ware, Mass.; Middlesex College of Medicine and Surgery, Waltham, 1933; member of the American Academy of General Practice; veteran of World War II; associated with the Mary Lane Hospital, where he died March 23, aged 51, of myocardial infarction.

Lewis, Sigma Van, Garner, N. C.; Medical College of Virginia, Richmond, 1916; veteran of World War I; for many years associated with the North Carolina State Board of Health and the U. S. Public Health Service; died March 17, aged 68.

Lewis, Ulysses Simpson Ⓜ East Dubuque, Ill.; Rush Medical College, Chicago, 1896; served as mayor; for many years surgeon for the Illinois Central and Chicago, Burlington and Quincy railroads; on the staffs of Finley Hospital and St. Joseph Mercy Hospital, Dubuque, Iowa, where he died March 20, aged 93, of coronary occlusion.

Leyden, Horace Alma, Anniston, Ala.; University of Tennessee College of Medicine, Memphis, 1909; veteran of World War I; member of the Anniston Chamber of Commerce; associated with the Anniston Memorial Hospital, where he died March 26, aged 73, of cerebrovascular accident.

Litton, Louis Ⓜ Chicago; University of Illinois College of Medicine, Chicago, 1924; on the staff of the Louis A. Weiss Memorial Hospital; died in the Mount Sinai Hospital April 10, aged 65, of acute myocardial infarction.

Lloyd, Claude Allen Ⓜ Washington, Ind.; Rush Medical College, Chicago, 1901; for many years local physician for the Baltimore and Ohio Railroad; died March 19, aged 84, of carcinomatosis of the sigmoid colon.

Logan, Leslie Ⓜ Barbourville, Ky.; Louisville and Hospital Medical College, Louisville, Ky., 1908; died in St. Joseph Infirmary, Louisville, April 1, aged 79, of cerebral thrombosis.

McCord, James Robert Ⓜ Ocala, Fla.; born in Conyers, Ga., Aug. 27, 1884; Jefferson Medical College of Philadelphia, 1909; specialist certified by the American Board of Obstetrics and Gynecology; member of the American Gynecological Society; fellow of the American College of Surgeons; past-president of the American Association of Obstetricians and Gynecologists; first president of the South Atlanta Association of Obstetricians and Gynecologists, which he helped found; secretary of the Section on Obstetrics, Gynecology and Abdominal Surgery, American Medical Association, from 1931 to 1934 when he became chairman, serving until 1935; fellow of the American College of Surgeons; formerly professor of gynecology and obstetrics at Emory University School of Medicine in Atlanta; for several years conducted extension courses in obstetrics throughout the United States in his capacity as senior medical officer and special representative of the Children's Bureau of the U. S. Department of Labor; veteran of World War I; in 1946 awarded an honorary doctor of science degree by Emory University and in 1959 was honored by the Medical Alumni Association of Emory for his contributions to medical education; died in the Munroe Memorial Hospital March 26, aged 75, of heart failure and arteriosclerotic heart disease.

McCulloch, Ernest Chester, De Land, Fla.; Ohio-Miami Medical College of the University of Cincinnati, 1910; in 1922 retired from the regular Army as a lieutenant colonel; physician to the Procter and Gamble Company at Staten Island, N. Y., until 1951; died April 2, aged 73, of pulmonary emphysema.

MacDonald, Ranald Forrest III Ⓜ Montvale, N. J.; St. Louis University School of Medicine, 1952; interned at the Hackensack (N. J.) Hospital, where he was a member of the staff; died in New York City March 23, aged 32.

McWilliams, Charles Terrell, Springhill, La.; University of Louisville (Ky.) Medical Department, 1910; died March 24, aged 75, of a heart attack.

Martin, Gideon Micajah, Meridian, Miss.; Mississippi Medical College, Meridian, 1908; died March 23, aged 82.

Martin, Robert Edwin Ⓜ Providence, R. I.; Cornell University Medical College, New York City, 1946; interned at the Rhode Island Hospital, where he served a residency; served a residency at the Providence Lying-In Hospital; specialist certified by the American Board of Obstetrics and Gynecology; certified by the National Board of Medical Examiners; served in the medical corps of the U. S. Naval Reserve; formerly associated with the Veterans Administration Hospital; died in Sebring, Fla., March 23, aged 37, of coronary thrombosis.

Masenhimer, Harry Walter, Lakewood, Ohio; Johns Hopkins University School of Medicine, Baltimore, 1908; associated with the Lakewood (Ohio) Hospital and the Fairview Park (Ohio) Hospital, where he died March 23, aged 77, of cerebral arteriosclerosis.

Miles, Martin Bernard, Boulder, Colo.; University of Colorado School of Medicine, Denver, 1931; fellow of the American College of Surgeons; veteran of World War II; past-president of the Boulder County Medical Society; associated with the Community and County of Boulder General hospitals; died March 15, aged 56, of carcinomatosis and bronchogenic carcinoma.

Moe, Leonard Nicholas, Jacksonville, Fla.; University of Nebraska College of Medicine, Omaha, 1925; member of the American Academy of General Practice; interned at St. Luke's Hospital in Jacksonville; chief surgeon for the Seaboard Air Line Railroad; died March 25, aged 60.

Mosely, Mack Joseph Jr. Ⓜ Galveston, Texas; Meharry Medical College, Nashville, Tenn., 1944; interned at the Homer G. Phillips Hospital in St. Louis, where he served a residency; staff member of St. Mary's Infirmary; recent recipient of the Eli Lilly Medical Research Laboratory Award; died in the John Sealy Hospital March 23, aged 37, of uremia.

Mulvany, Thomas Anthony, San Francisco; Marquette University School of Medicine, Milwaukee, 1943; interned at St. Mary's Hospital in San Francisco; died March 26, aged 44.

Neafie, Charles Allen Ⓜ Pontiac, Mich.; born in 1882; University of Maryland School of Medicine, Baltimore, 1909; specialist certified by the American Board of Preventive Medicine; past-president of the Oakland County Medical Society and in 1956 received its seventh annual award for "distinguished service to medicine"; served as treasurer of the Michigan Health Officers' Association; for many years health officer of Pontiac; for eight months in 1933 deputy director of the Maine Department of Health and Welfare; in 1912 resident physician at the Pontiac State Hospital; served on the staff of the Pontiac General Hospital, where he was medical director for three years; died March 23, aged 77.

Pelzig, Alfred, Forest Hills, N. Y.; Middlesex University School of Medicine, Waltham, Mass., 1943; certified by the National Board of Medical Examiners; specialist certified by the American Board of Dermatology and Syphilology; instructor of clinical dermatology and syphilology, New York University Post-Graduate Medical School; assistant surgeon in the U. S. Public Health Service Reserve, 1945-1946, and later served in the Korean War; associate attending dermatologist at the University Hospital; died in the Horace Harding Hospital in Elmhurst March 21, aged 40, of acute myocardial infarction.

Reiss, Henry Ⓜ New York City; Columbia University College of Physicians and Surgeons, New York City, 1900; died in Miami Beach, Fla., March 10, aged 82.

Richardson, James Lee, Ashland, Ky.; Eclectic Medical Institute, Cincinnati, 1899; on the honorary staff, King's Daughters' Hospital, where he died March 23, aged 88, of obstruction to the common bile duct.

Roessler, Harry Keer Ⓜ Ambler, Pa.; Hahnemann Medical College and Hospital of Philadelphia, 1905; for many years on the staff of St. Luke's and Children's Medical Center in Philadelphia; died in the Abington (Pa.) Memorial Hospital; died March 28, aged 79, of retroperitoneal hemorrhage.

Rosenfeld, Arthur Samuel Ⓜ Portland, Ore.; Johns Hopkins University School of Medicine, Baltimore, 1911; veteran of World War I; interned at the Mount Sinai Hospital in New York City; for many years on the faculty of the University of Oregon Medical School; staff member of the Good Samaritan Hospital; died March 20, aged 74, of coronary occlusion.

Rothrock, Francis Blake Ⓜ Colorado Springs, Colo.; Missouri Medical College, St. Louis, 1899; died in St. Francis Hospital March 19, aged 84, of coronary thrombosis.

Rysanek, William J., Baltimore; born Sept. 28, 1883; Maryland Medical College, Baltimore, 1905; in 1955 at a dinner honoring his 50th anniversary of general practice, received special greetings from Mayor D'Alesandro, who designated him as "an honored and outstanding citizen of Baltimore," and Dr. Huntington Williams, commissioner of health, who wrote "Such a splendid life of unselfish devotion to the many fortunate persons who have come under your care during these many years is an inspiration to all of us and is a cause for rejoicing on the part of the city of Baltimore"; served on the staffs of Franklin Square Hospital, St. Joseph Hospital, and Church Home and Hospital, where he died March 28, aged 76, of uremia.

Samostie, Joseph M., Long Beach, N. Y.; University of Moscow Faculty of Medicine, Russia, 1917; Friedrich-Wilhelms-Universität Medizinische Fakultät, Berlin, Prussia, Germany, 1923; died Feb. 22, aged 67, of coronary occlusion.

Sanchez Castano, Fructuoso Ⓜ Santurce, P. R.; Georgetown University School of Medicine, Washington, D. C., 1923; member of the House of Delegates of the American Medical Association from 1949 through 1957 and in 1959; died March 2, aged 62, of cancer.

Sargeant, Stanley Constantine, Crownsville, Md.; Howard University College of Medicine, Washington, D. C., 1947; interned at the Harlem Hospital in New York City; served a residency at the Norwich (Conn.) State Hospital and served a fellowship at the Freedmen's Hospital in Washington, D. C.; attached to the staff of Crownsville (Md.) State Hospital; died March 18, aged 38.

Settino, Joseph J., Pittsburgh; Loyola University School of Medicine, Chicago, 1931; served as physician for the Sharpsburg public schools; retired as physician for the Baltimore and Ohio Railroad; staff physician at St. Francis General Hospital, where he died March 17, aged 55, of acute dissecting thoracic aortic aneurysm.

Shapiro, William Mordecai, Toledo, Ohio; University of Wooster Medical Department, Cleveland, 1913; specialist certified by the American Board of Radiology; veteran of World Wars I and II; formerly county coroner; on the staff of St. Vincent's Hospital, where he died March 21, aged 69, of right cerebral vascular accident.

Shearer, Floyd Eugene Ⓜ Edgerton, Wis.; Marquette University School of Medicine, Milwaukee, 1913; veteran of World War I; vice-president and chairman of the board of the Tobacco Exchange Bank; on the staff of St. Mary's Hospital in Columbus and the Memorial Community Hospital, where he died March 25, aged 70, of acute coronary insufficiency.

Shorts, William Francis, Wishram, Wash.; Maryland Medical College, Baltimore, 1911; also a pharmacist; died in Spokane Feb. 27, aged 76, of cancer of the prostate with metastases.

Stein, Emil Ⓜ Elizabeth, N. J.; University and Bellevue Hospital Medical College, New York City, 1906; fellow of the American College of Surgeons; formerly member of the board of education and in 1934 served as vice-president; served as president of the board of health; associated with the Alexian Brothers Hospital, St. Elizabeth Hospital, and the Elizabeth General Hospital, where he died March 26, aged 76.

Stern, Frederick D. Ⓜ New York City; born in Wiesbaden, Germany, Feb. 27, 1897; Julius-Maximilians-Universität Medizinische Fakultät, Wurzburg, Bavaria, Germany, 1924; served a residency at the Montefiore Hospital for Chronic Diseases; specialist certified by the American Board of Psychiatry and Neurology; member of the American Academy of Neurology, American Psychiatric Association, and the Association for Research in Nervous and Mental Diseases; served on the faculty of Columbia University College of Physicians and Surgeons; chief of neurology in the regional office of the Veterans Administration; associate attending physician, division of neurology, Montefiore Hospital, where he died April 8, aged 68.

Strachstein, Abraham, New York City; Cornell University Medical College, New York City, 1908; member of the American Urological Association; served on the faculty of his alma mater and the Columbia University College of Physicians and Surgeons; associated with the Beth Israel Hospital, where he died April 3, aged 79, of heart failure.

Turner, William Barron, Kershaw, S. C.; Medical College of the State of South Carolina, Charleston, 1912; Kershaw County superintendent of education for two terms, 1904-1908; for many years trustee of the Kershaw County Board and trustee of the city schools; died in the Camden (S. C.) Hospital March 18, aged 89.

Walker, Scioto Pierce, Huntington, W. Va.; Maryland Medical College, Baltimore, 1911; served on the medical board of St. Mary's Hospital; died March 26, aged 82, of probable coronary occlusion.

Ware, Thomas Hendrix, Seminole, Okla.; Memphis (Tenn.) Hospital Medical College, 1912; died in the Baylor University Center, Dallas, Texas, March 7, aged 74, of chronic pyelonephritis and uremia.

Wessell, John Charles Ⓜ Wilmington, N. C.; born in Wilmington Sept. 19, 1877; University of Maryland School of Medicine, Baltimore, 1900; formerly associated with the U. S. Public Health Service; consulting physician and surgeon for the Atlantic Coast Line Railroad Company; a director of the North Carolina Tuberculosis Association; recipient of a bronze medallion issued by the National Tuberculosis Association; member emeritus of the Consolidated Board of Health, of which he was an active member for many years; associated with the James Walker Memorial Hospital; for six years served on the board of trustees of the Community Hospital; died March 20, aged 82, of cancer of the prostate.

West, Davenport Ⓜ New York City; Columbia University College of Physicians and Surgeons, New York City, 1909; for many years associated with the Roosevelt Hospital; veteran of World War I; an examining physician for selective service boards during World War II; died in Nassau, Bahamas, March 30, aged 77.

Wood, John Raymond, Wadena, Iowa; the Hahnemann Medical College and Hospital, Chicago, 1911; served as county coroner; died in the Veterans Administration Hospital, Iowa City, March 11, aged 72, of lobular pneumonia.

Youngs, Amos Sylvester Ⓜ Kalamazoo, Mich.; Michigan College of Medicine and Surgery, Detroit, 1896; died March 26, aged 89.

FOREIGN LETTERS

BRAZIL

Plasma Volume in Malnourished Patients.—The increase in plasma volume in patients not affected by diseases associated with hypervolemia (congestive heart failure, renal insufficiency, hyperthyroidism, and hepatic cirrhosis) has not been widely studied. Dr. F. Paulino (*Rev. brasil. med.* 16:842, 1959) analyzed a series of 300 surgical patients with malignant tumors, chronic infection, and malnutrition. This study led to the recognition of two types of abnormal volemia: that in which blood volume is reduced due to a reduction of cells and plasma and that which has dissociated volemia with decreased or normal cell volume and increased plasma volume. The latter type is not rare and was observed by the author in 20 to 35% of patients with cancer of the stomach, esophagus, colon, and lungs.

Several emaciated and malnourished patients with malignant tumor or chronic infection had anemia manifested by decreased cell volume and increased plasma volume. The mechanism of this increase is not known. The author observed a progressive decrease of the plasma volume after blood transfusions given with such other preoperative measures as adequate diet, rest, and antibiotics. During treatment, beside the marked fall in the plasma volume, an increase of the diuresis, a loss of weight, and an improvement in general condition were observed. The serine level, in general low, increased during treatment, so that it was not convenient to give blood cell transfusions to these patients.

The author emphasized that the increase in plasma volume had no relationship to the fall in the number of blood cells, since in patients with malignancies and continuous hemorrhage the anemia persisted and the plasma volume was progressively reduced. This last fact seemed to favor the hypothesis that the expansion of the vascular space, caused by the increase in plasma volume, depended on general factors unrelated to the anemia. The author believed that expanded plasma volume might not be related to hypoglobulinemia but to an alarm reaction to the disease itself.

Changes in Body Weight After Partial Gastrectomy.—Dr. D. P. Neves and co-workers (*Rev. Hosp. clin.* 14:434, 1959) studied a series of 618 patients who had had a partial gastrectomy. In this study the body weight after the operation was expressed as a percentage in relation to the preoperative weight with the admission that a 5% increase or decrease was without significance. All patients were classified as (A) being clinically well or without symptoms after meals; (B) having postprandial nausea, pain, vomiting, heartburn, belching, tachycardia, dizziness, or meteorism; or (C) having only diarrhea. Group A consisted of 233 patients (37.8%), group B of 355 (57.4%), and group C of 30 (4.8%).

A loss of weight was observed in 303 patients (49.0%), in 100 (16.2%) there was an increase in weight, and 215 (34.8%) showed no change. Trying to correlate the changes in weight with the symptoms, the authors found that of the patients in group A, 75 (32.2%) had an increase in weight, 43 (18.4%) had a decrease, and 115 (49.4%) had no change. Of the patients in group B, 19 (5.3%) showed an increase in weight, 248 (69.9%) showed a decrease in weight, and 88 (24.8%) showed no change. In group C, 6 patients (20%) showed an increase in weight, 12 (40%) showed a decrease in weight, and 12 (40%) showed no change. The authors, therefore, concluded that the loss of weight was more closely related to postprandial symptoms than to diarrhea.

Nylon Graft in Abdominal Wall.—Montoro and Gentil (*Rev. Paulista med.* [Jan.] 1960) used nylon grafts in three patients in the repair of the abdominal wall after radical resection for neoplastic diseases. In two patients the graft was used after herniation occurred. In the third patient it was used immediately after resection of the abdominal wall. In all three patients good results were obtained; there was no recurrence of the herniation, nor was there any wound infection. The only postoperative complication was a moderate amount of serous drainage. The nylon graft appeared to be as good as tantalum, and it had the advantage of being easily obtainable.

DENMARK

Sciatica.—Dr. E. S. Staffeldt (*Ugesk. laeger*, Feb. 25, 1960) compared two groups of patients, each numbering 100, who suffered from sciatica and who received different kinds of treatment at different times at the same hospital. The first group was admitted to the medical side of the Aarhus general hospital during the period 1938 to 1942. Therapy consisted of prolonged, strictly enforced rest in bed, warmth, and massage, but no exercises. The second group was admitted to hospital during the period September, 1949, to April, 1951. Meanwhile there had been a radical change in treatment, the second group undergoing much more

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The items in these letters are contributed by regular correspondents in the various foreign countries.

active measures. After a week of confinement to bed, to an extent largely determined by the degree of Lasegue's sign and the severity of other symptoms, the patients were given exercises designed to relax the muscles involved without any strain being imposed on the spine. Respiratory exercises were also prescribed with a view to promoting costoabdominal respiration.

To combat myositis of the lumbar and gluteal muscles, warmth was applied in the form of electric pads for a half-hour twice daily. Before discharge from hospital, the patients were taught how to work and lift most effectively. The two groups were compared according to the duration of their stay in hospital (50 days for the recipients of conservative treatment and 30 days for the active group) and according to their condition on discharge. Though the two groups may not have been strictly comparable, they resembled each other closely enough to warrant the conclusion that prolonged rest in bed should not be the standard method of treatment for the sciatica syndrome.

Dipsomania.—The successes achieved with disulfiram in the treatment of dipsomania led, in 1950, to the creation of an ambulatorium in which the drug could be administered. Since then this institution has treated 1,185 patients. According to Dr. H. Ehler (*Ugesk. laeger*, Feb. 18, 1960) its staff of one physician, one social worker, and two volunteer assistants is so busy that it can hardly cope with the 100 or more patients coming to it yearly. The early enthusiasm over disulfiram has waned. The dosage has been reduced and a more sober but still appreciative attitude to it has been adopted. This reduction of dosage to 500 mg. twice a week, in tablet or mixture form, has led to the cessation of the side-effects provoked by the earlier, more heroic dosages. Chlorpromazine and Serpasil have been superseded by perphenazine administered in 1959 to 36 patients in doses of 4 to 8 mg. daily for periods never exceeding 45 days at a time. It has proved remarkably effective in combating the psychopathic dysphoria to which many dipsomaniacs are prone.

Much of the success achieved by physician-patient dialogues hinged on the physician's approach and the patient's reaction on the first occasion, and experience has taught the former to leave the initiative as much as possible to the latter. Ehlers has little enthusiasm for the constitution of groups among his patients, because the tone of conversations within such groups is not always wholesome.

Soybean Oil and Serum Cholesterol.—Dr. T. Geill and co-workers (*Ugesk. laeger*, Feb. 18, 1960) studied the influence of a diet low in fat but rich in soybean oil on the serum cholesterol level of the inmates of a home for elderly persons. Without any noticeable inconvenience to 24 women and 18 men aged 62 to 94 years, their ordinary hospital diet was changed so that it contained only 20 Gm. of animal fat, while 50 Gm. of a soybean oil was given, mainly as margarine. A soybean oil milk was prepared as an emulsion in skimmed milk. The total serum cholesterol content was then determined. This experiment lasted eight weeks. Before it was started, the mean serum cholesterol level was 232 mg. per 100 ml. for women and 175 mg. per 100 ml. for men. At first there was a rapid, and later a slower, fall of the serum cholesterol level, which returned to normal on the resumption of the original diet.

Iproniazid for Psychiatric Ailments.—Jensen and Kodahl (*Nord. med.* March 10, 1960) gave iproniazid to two different categories of patients. The first group included 27 patients admitted to the psychiatric department of the Copenhagen City Hospital who were given this drug for more than a month. In addition to 9 patients with endogenous mental depression there were 2 with depressive neurosis, 12 with senile or presenile depression, and 4 who had arteriosclerotic dementia with depression. The dosage was 100 to 200 mg. daily. This was increased in a few patients to 300 mg. daily. In 13 patients the improvement observed was completely satisfactory and in 3 others only moderately so. In 11 no improvement was noted. The second category included 20 ambulant patients who were also given iproniazid for a month or more. Apart from two neurotic patients on whom the drug seemed to have no effect, the reactions to it were encouraging, and in a pseudoneurotic schizophrenic patient with severe and persistent depression the symptoms vanished after the drug had been administered for two days. The reactions were of two types: they might be prompt, within 2 or 3 days, or delayed and gradual, after 10 to 15 days. There were only a few side-effects, such as slight giddiness, constipation, and headache. The improvement the drug could effect was often so great that it compared well with electroshock at its most successful.

Renal Function and Chronic Polyarthritis.—Dr. A. W. S. Sörensen (*Ugesk. laeger*, March 17, 1960) investigated the renal functions of 153 patients with chronic polyarthritis. Serving as controls were 200 patients with other diseases. The ages of the polyarthritic group were 15 to 82 years, and the mean duration of their polyarthritis was 11 years. The ages of the control group were 17 to 83 years. Many of the polyarthritic patients had been treated with gold, steroids, ACTH, phenylbutazone, or acetophenetidin over long periods. The renal function was tested by the three-day creatinin clearance method, and the average figures obtained for the control group were regarded as normal. While only 10.5% of the controls showed reduced renal function, this reduction was observed in 33.3% of the polyarthritic group and the incidence of the condition rose markedly with the severity of the polyarthritis. No correlation could be established between the reduction of renal function and treatment with steroids, ACTH, gold, phenylbutazone, or acetophenetidin.

FRANCE

Hepatosplenomegaly.—Payet and Armengaud (*Presse méd.* 67:2128, 1959) studied a series of Africans who had hepatosplenomegaly due to (1) tuberculosis, typhoid, cardiac disease, or hemopathy that regressed following specific therapy; (2) malaria, schistosomiasis, or syphilis; (3) an unknown origin such as an unrecognized cause of nutritional imbalance or infection. (A number of such patients might have had malaria, schistosomiasis, or trypanosomiasis in childhood.) Hepatosplenomegaly seemed always to be associated with diseases predominantly involving the reticuloendothelial system. Experiments on animals have shown that the blocking of the reticuloendothelial system produces round cell infiltrations with alteration of the electrophoretic pattern indicative of the presence in the blood of macromolecules of exogenous or endogenous origin. The hepatic aspect of this condition has been exaggerated at the expense of the reticuloendothelial aspect. Hepatosplenomegaly may disappear spontaneously or as a result of treatment, or it may be irreversible. In patients with the irreversible type splenectomy must be considered.

Serum Transaminase and Aldolase Levels and Myopathy.—Breton and co-workers (*Presse méd.* 67:2329, 1959) stated that increased serum transaminase and aldolase levels early in the course of a disease strongly suggested a myopathy. At this stage these tests are of great diagnostic value. In a young child, greatly increased levels of these enzymes confirm the presence of myelopathic muscular atrophy. Low values rule out this condition. In older children the same is generally true, but subnormal levels of these enzymes do not exclude the diagnosis. On the contrary, the amyotrophy is not of neurogenic origin if the transaminase and aldolase levels are not definitely increased.

Having recognized the most common causes of error, such as hepatic disease and certain isolated modifications of aldolasemia, as found in rachitic patients, for example, it is relatively simple to avoid errors of interpretation if several successive analyses of various enzymes are performed. Some observers believe that increased values indicate an unfavorable prognosis. Pearson, however, believes that they indicate a rapid dystrophic course without relation to the eventual severity of the amyotrophy. The importance of enzyme studies should be borne in mind each time a new drug is tried. Evaluation of aldolase and transaminase levels during a given treatment will permit appreciation of its usefulness. A specific drug should reduce enzymatic elimination, but this criterion is of value only if the treatment is given early in the course of the disease.

Streptomycin and Hydrostreptomycin Methionates.—Almeida and Almeida (*Presse méd.* 67:2337, 1959) stated that 20% mixtures of streptomycin methionate and hydrostreptomycin methionate with sulfates (M 20) were less toxic than the 20 or 50% mixtures of pantothenates of these antibiotics. M 20 has the advantages that it is cheaper than the pantothenates and is better tolerated locally.

Secondary Hyperaldosteronism.—Warter and co-workers (*Presse méd.* 68:5, 1960) determined the aldosterone concentration in the urine of 59 patients with essential hypertension. Twelve of these showed evidence of hyperaldosteronism. The urinary aldosterone levels were 10 to 30 mcg. in 24 hours. In none of the patients was Conn's syndrome observed. In one patient with a clear-cut hypokalemia, the hypertension was definitely of renal origin. Therefore, hypertension, hypokalemia, and hyperaldosteronuria are not sufficient criteria for the diagnosis of Conn's syndrome. A patient with high blood pressure may manifest hyperaldosteronism even when a moderate salt restriction, which would not affect a normal subject, is imposed. Such hyperaldosteronism makes any sodium intake in these patients dangerous.

Alpha-Chymotrypsin in Plastic Surgery.—Dufourmental and co-workers (*Presse méd.* 68:213, 1959) studied the action of alpha-chymotrypsin in 47 patients who had had plastic operations. The drug was given intramuscularly in a daily dose of 5 mg. for three or four postoperative days. In some patients the treatment was continued for two weeks. The drug greatly reduced postoperative swelling, favored the cicatrization and good nutrition of the flaps, and prevented venous thrombosis.

Loeffler's Syndrome.—H. Boucher and co-workers (*Presse méd.* 68:57, 1960) stated that in Europe Loeffler's syndrome is often due to ascariasis. It is, however, sometimes difficult to prove the presence of the parasite. Loeffler's syndrome is associated with an incomplete parasite life-cycle (absence of ova in the stools). This may be due to infestation with an ascaris from a lower animal, and therefore not viable in man, or with a human ascariasis that runs an abbreviated course. The larvae of the ascaris species commonly found in pigs, dogs, or cats die rapidly within the human intestine. Also, because of a kind of immune reaction frequent in adults, the system gets rid of parasitic larvae quickly. In a series of 41 case histories the authors show that ascaridic Loeffler's syndrome with incomplete parasite life-cycle is by far the most frequently seen Loefflerian lesion, at least in adult patients. For this reason skin testing with a lyophilized antigen is a valuable diagnostic aid in such cases.

Pulmonary Tuberculosis.—E. Bernard and co-workers (*Presse méd.* 68:209, 1960) compared the results obtained in a group of adult patients with pulmonary tuberculosis treated daily with 15 mg. of isoniazid per kilogram of body weight and in an analogous group given the usual daily dose of 5 mg. per kilogram. The patients in both groups were also given a daily dose of 15 Gm. of PAS intravenously. At the end of three months of treatment, roentgenograms indicated marked improvement in patients receiving the larger dosage. This advantage was most apparent in the patients with extensive or cavitary lesions but was less evident in those with infiltrative or nodular lesions. A more rapid and frequent cure was obtained with the larger dosage. Tolerance to the larger dosages was satisfactory. In only one patient was it necessary to discontinue the treatment. The authors believed that the neuropsychical manifestations attributed to isoniazid were observed only in subjects with a previous history of neurosis. In all other subjects such manifestations were rare and did not constitute a contraindication to the use of the increased dosage.

Rehydration.—A. Avachian (*Presse méd.,* Dec. 26, 1959) devised an apparatus for aspirating body fluids in infants with stasis and for perfusing various therapeutic solutions in those with severe toxicosis, uremic coma, and surgical ileus. He introduced two tubes into the nostrils. The first was passed into the jejunum, and the other tube remained in the stomach with its tip about 2 cm. below the cardia. The two tubes were fixed to the upper lip with adhesive tape and were connected with an apparatus which possessed two circuits for gastric and intestinal perfusion. With the aid of the two tubes the author performed gastric and intestinal lavage, followed by aspiration of the diluted body fluids (resulting from stasis). After controlling the gastric and intestinal pH level, he proceeded with the therapeutic perfusion.

The total amount of fluid indispensable for rehydration was calculated according to the weight of the infant and the degree of dehydration. A surplus of 10% may be added to compensate for the volume of fluid aspirated. The author began with a rapid rehydration for four to six hours, in the course of which he perfused 30 to 40% of the total amount of fluid. In the second stage, maintenance perfusion was given at a slower rate. By way of the intestinal tube, he introduced antibiotics, plasma, and vitamins, according to the infant's needs. In 364 infants treated by this method, the case fatality remained below 15%.

Determination of Biliary Debit.—J. Stalport and co-workers (*Lyon chir.,* Nov., 1959) devised an apparatus for measuring the function of Oddi's sphincter in the course of an operation. For this examination the common bile duct is perfused by means of transcystic catheterization. The apparatus used includes a rotameter of paraffin oil and an electronic relay which insures the amplification of the graphic transmission. Tracings are studied before and after the intravenous injection of succinylcholine. A normal tracing at the start represents a debit of 1 cc. per minute for a pressure between 10 and 17 cc. of isotonic sodium chloride solution. The debit is subjected to rhythmic variations which may be observed in the tracing. These variations depend on the respiratory movements, the peristaltic waves moving through the biliary passages, and the rhythmic opening and closing of the biliary duct.

After the injection of succinylcholine, which causes a dilatation of Oddi's sphincter, there is a sudden change in the direction of the tracing. This inflexion is constant when the biliary passages are unimpaired. The biliary passages may be classified as normal, hypotonic, or hypertonic, according to the pressure required for obtaining a debit of 1 cc. per minute. The succinylcholine test reveals the presence of an organic obstruction. It also makes it possible to differentiate between an organic and a functional obstruction. In case of obstruction due simply to hypertonia of Oddi's sphincter, the injection of succinylcholine produces a marked dilatation.

Levomepromazine for Refractory Pain.—J. Sigwald and co-workers (*Therapy,* no. 6. 1959) studied a series of 12 patients who had neuralgia of the trigeminal nerve refractory to all the usual methods of treatment. Ten patients were treated with complete success by the administration of levomepromazine. Treatment was started with a dosage of 100 mg. per day, given in divided doses. The daily dosage then was increased to 300 mg. and in some patients to 750 mg. As soon as improvement became manifest, the dosage was gradually reduced to avoid a sudden withdrawal of the drug. In patients with refractory facial neuralgia, either primary or secondary to an operation on the gasserian ganglion, much improvement was obtained, but the treatment should not be interrupted or a relapse may occur.

Of 22 patients with pain caused by cancer, and refractory to the administration of morphine and surgical treatment, 12 obtained excellent and 8 obtained good results. Good results were also observed in patients with pain caused by tabes dorsalis, in patients with phantom limb, and in those with thalamic syndrome. The drug may be given intramuscularly at first, and after improvement has been obtained it may be given by mouth. This treatment should be given only to patients who are hospitalized.

GERMANY

The Silent Gallstone.—E. Bock and H. Henning (*Ärztl. Wchnschr.* 14:943, 1959) stated that on the basis of pathological findings it may be supposed that 10% of adult men and about 25% of adult women have gallstones that cause few if any symptoms. Only 50% of such patients remain symptom-free after cholecystectomy. Conservative treatment is, therefore, preferred, and operation should be considered only when conservative measures fail. Clear-cut indications for operation are repeated attacks of colic and icterus, and the first bout of fever makes a relative indication into an absolute one.

To arrive at a better judgment of the indications for operation, the authors made a catamnestic investigation of 224 patients (207 women and 17 men). In 142 of them the presence of cholelithiasis was confirmed by x-ray and in the rest it was deemed highly probable from the history and clinical findings. In 8 patients the cholelithiasis was detected by chance, but in 139 its history could be traced for up to five years. Considering 20 to 30 years as the typical age for the development of cholelithiasis, and taking into account that the average age of the observed patients was 55 to 60 years, it appears that the gallstone carrier in many cases develops symptoms only after a latent period of two or three decades. Of the 224 patients 78 were operated on because of continuously recurring colic, fever, and icterus, and 21 refused operation. Since the indication for cholecystectomy was related not only to the type of biliary disease but also to the general operative risk, the number of operations remained comparatively low.

In this series 130 patients were followed up for three to seven years after conservative treatment. Of these 10 had died, but the biliary disease was not a proved contributor to their death. The patients were divided into three groups according to their symptoms. Group 1 had colic only; group 2 had colic, fever, and icterus; and group 3 was symptom-free. In the follow-up examinations attention was paid to such factors as recurrence of colic, icterus, and fever, to observation of diet, and to possible later necessity for cholecystectomy. After three to seven years 53 patients (40%) were symptom-free, and 77 had a recurrence of biliary symptoms. In 12 of the symptom-free patients a solitary stone was found; in 16 the cholecystogram showed no stones; and in the other 25 multiple stones were seen.

Thirty-one patients of the group had not observed a special diet. Of the eight in whom gallstones were found only by chance, three later had colic but no further complications. Of 21 patients who had been advised to have a cholecystectomy only 6 had had to be operated on although 13 had bouts of colic. The authors concluded that, by itself, detection of gallstones is not an indication for operation, if only because development of an inflammation may often be related to a second disease. Only when this second disease occurs with frequent attacks of pain, fever, or congestive icterus does the need for cholecystectomy become acute. On the other hand, operation is inevitable when, in spite of intensive conservative treatment, painful attacks or congestive icterus occur and a complicating hepatic or pancreatic affection appears.

Oral Test for Pregnancy.—Igel and Enold of Berlin (*Med. Klin.* 54:1460-1462, 1959) stated that the administration of progesterone to patients with primary or secondary amenorrhea is expected to produce bleeding, while it has no such effect on patients who are pregnant. Recent studies were designed to find out whether a preparation consisting of 5 mg. of methylestrenolone and 0.5 mg. of methylestradiol per tablet would be a suitable test for pregnancy. After the rat-estrus test had been made on a series of 101 women in whom pregnancy was suspected the patients were given 1 tablet and 24 hours later another tablet of the preparation. Of these women 62 were pregnant, and the result of the rat-estrus test agreed with the result of the oral test (no bleeding occurred) in 60.

In one patient the preparation caused slight bleeding which had no effect on the pregnancy. Her rat test had given a positive result. In another patient the biological test gave a negative result and the oral test a positive result. Menstruation was overdue for only five days. Of the other 39 patients 34 reacted with bleeding for 1 to 10 (average 4) days after taking the tablets. In these patients the rat-estrus test gave negative results. In the other five the oral test gave false-positive results. Bleeding failed to occur because of amenorrhea existing for more than three months. The reliability of the oral test is, therefore, excellent when secondary amenorrhea can be excluded.

Poisoning from Nose Drops.—A report of the Drug Commission (*Ärztl. Mitteilungen*, no. 2, p. 69, 1960) stated that in recent years poisoning in infants and small children due to overdosage with nose drops and nasal sprays containing naphthylimidazole has been repeatedly observed. Overdosage with such preparations may cause marked and even life-threatening disturbances of the respiratory center, collapse, and somnolence. In order to prevent such accidents the commission recommends that (1) these preparations should not be used as sprays for infants and children below 6 years of age because the exact therapeutic dosage is difficult to determine and the danger of overdosage is great, and (2) if naphthylimidazoline drops must be used for infants and children under 6 years of age they should not be stronger than 0.05% (a dilution 1:2,000), because with a concentration of 1:1,000 there is too much danger of an overdose.

The commission urgently requested pharmacists to advise customers accordingly when dispensing such preparations. It also recommended that the makers of nose drops and sprays containing naphthylimidazole should state in a prominent place on the package of such drops and sprays when they contain a 0.1% solution that this strength is suitable only for adults and children over 6 years of age. They should also equip packages of 0.05% drops with pipets which hold no more than one drop in order to preclude overdosage.

Peridural Anesthesia.—H. Klosterhalfen of Düsseldorf (*Ztschr. Urol.* 52:84-89, 1959) used levopromazine on 164 patients as a basic depressor and N-(3 dimethylaminopropyl) phenothiazine for potentiation prior to the beginning of an operation. Levopromazine has potent antihistaminic action. Its central effect is 30 to 50% greater than that of the previously used chlorpromazine. It has about the same effect on the autonomic nervous system, while its secretion-inhibiting properties are less. Levopromazine lowers the blood pressure by 20 to 25% in the average patient and in hypertensive patients by up to 40%.

One hour before operation patients were given a mixed injection containing 50 mg. of levopromazine, 25 mg. of promethazine, and 50 mg. of diphenylhydantoin intramuscularly. This injection also sufficed for younger patients who did not satisfactorily respond to chlorpromazine premedication. Side-effects were swelling of the nasal mucosa and conjunctival injection. N-(3 dimethylaminopropyl) phenothiazine proved suitable for ganglionic blocking immediately before operation. It has only slight peripheral and central action, hardly affects circulation, and is well tolerated on intravenous injection, thus providing for short-term and individually controlled potentiation. Patients were given one or two ampuls (20 or 40 mg.) of 1% solution, one ampul of strong preparation (50 mg.) intravenously, or a combination with diphenylhydantoin. The injection was given very slowly. Circulation and blood pressure were affected in only 2 of the 164 patients, which contrasted well with results after chlorpromazine premedication. Sympathicomimetics are contraindicated because of the danger of epinephrine reversal.

INDIA

Tuberculosis Survey.—The national tuberculosis survey revealed that about 5 million people in India, or 1.3% of the population, suffer from pulmonary tuberculosis. The total number is thus much larger than was presumed. The number of infectious cases is probably at least 1,500,000, or 0.4% of the population. The fact that there is such a large number of infectious cases in urban and rural areas is a matter of serious concern and demands the highest priority for the antituberculosis campaign in the country's five-year plans. The survey has also belied the earlier assumption that the population in urban areas was more affected by tuberculosis than that in rural areas. For this reason, programs for control of tuberculosis have to be extended to rural areas also in the third and subsequent plans.

Grant for Malaria Control.—An additional grant of $665,550 has been authorized by the United States for India's malaria eradication program. A supplemental agreement signed in January by the government of India and the U. S. Technical Cooperative Mission provides special funds to procure chloroquine and primaquine phosphate tablets, jeeps, microscopes, slides, and calculating machines. These will further aid the eight-year-old Indo-U. S. efforts to banish malaria from India. The latest agreement brings the total of United States assistance to the malaria control and eradication program to $6,500,000.

Chlorpropamide.—C. J. Modi and co-workers (*J. Indian M. A.* 34:92 [Feb. 1] 1960) treated 10 patients with chlorpropamide for two months. All were elderly persons with moderately severe or severe diabetes. The duration of diabetes varied from less than one year to over 20 years.

The usual diet of the patients was continued during the trial. The drug was given in doses of 250 mg. twice daily for three days and then 250 mg. once daily in the morning. Five of the 10 patients were of normal weight, two were overweight, and three were underweight. One had received carbutamide earlier, four tolbutamide, one both carbutamide and tolbutamide, and three insulin. The maximum drop in fasting blood sugar level occurred in the first week, after which improvement was gradual. The normal value was reached in three weeks and was maintained. The mean 24-hour excretion of sugar fell 82%. Postprandial glycosuria was controlled in one week in three patients and in two to four weeks in others. No patient developed albuminuria at any stage, and microscopic examination of the urine showed no abnormality. The drug was well tolerated by all the patients, and, aside from the fall in the total leukocyte count seen in four patients, no side-effects were observed. The authors found chlorpropamide an effective and potent oral hypoglycemic agent. Five patients showed an excellent response and five a fair response.

Choline Theophyllinate for Cardiac Failure.—Datey and Sardesai gave choline theophyllinate as a diuretic agent to eight patients with congestive cardiac failure due to cor pulmonale, two with edema due to cirrhosis of liver, one with edema due to malnutrition, and three normal controls (*J. Postgrad. Med.* 6:33 [Jan.] 1960). The 11 patients with edema received a salt-poor diet containing 1.45 Gm. of sodium and 2.63 Gm. of potassium, and the controls received the regular hospital diet containing 7.15 Gm. of sodium and 2.87 Gm. of potassium. An average dosage of 0.75 Gm. of choline theophyllinate was given in 24 hours, and the dosage was increased to about 1.0 Gm. a day if there was no response. This dose was given orally and continued until the edema disappeared completely. Patients with congestive cardiac failure were first digitalized. If edema persisted in spite of the trial drug, 1 ml. of a mercurial diuretic was given intramuscularly.

Of the eight patients with congestive cardiac failure only one did not require mercurials. In the rest the response was inadequate when choline theophyllinate alone was given, but this agent greatly enhanced the diuretic response of the mercurial diuretic and enabled the frequency of the mercurial injections to be reduced. The patients with hepatic cirrhosis did not react so well. In the three normal controls no improvement in electrolyte excretion was seen after administration of the drug. Doses greater than 1 Gm. a day were not tolerated.

Needle Biopsy of Pleura.—M. D. Anjaria and co-workers (*J. Postgrad. Med.* 6:9 [Jan.] 1960) used needle biopsy of pleura in a series of 36 patients with fluid in the pleural space. Penicillin was used prophylactically in the first 19 patients, but as no infective complications were observed this therapy was discontinued. In 2 of these patients not enough tissue was obtained for examination, and in 12 the tissue obtained was not from the pleura. Of the remaining 22, histological examination suggested tuberculosis in 11, chronic inflammation in 10, and acute inflammation in 1. The authors find this method safe, quick, and simple, especially in diagnosing tuberculosis. There were no deaths or untoward complications in this series.

SGO-T and Coronary Heart Disease.—V. K. Dewan and co-workers (*J. Indian M. A.* 34:128 [Feb. 16] 1960) estimated serum glutamic oxalacetic transaminase (SGO-T) levels in a series of healthy adults, 5 patients with manifest liver disease, and 40 patients with coronary heart disease. The levels in the latter group were determined within 36 hours of their first clinical attack. In 17 of them electrocardiogram (ECG) showed typical changes of recent myocardial infarction, in 15 only equivocal changes were seen in ECG, and in 8 the ECG showed negative findings on two successive occasions. The average SGO-T level in normal controls was 41.4 units. In patients with liver disease this level varied between 52 and 67 units. The SGO-T level was higher than 65 units in all patients with heart disease and ranged between 65 and 322 units. In patients in whom the ECG was normal or showed only an ischemic pattern, a high SGO-T level helped confirm the clinical diagnosis of myocardial infarction. Patients with frank electrocardiographic changes of myocardial infarction showed much higher SGO-T levels than those with equivocal or negative findings. This estimation is of value in patients with coronary heart disease for confirmation of the clinical diagnosis, especially when the ECG findings are normal during the first two days of an attack.

JAPAN

Family Planning.—After more than 10 years the government-sponsored family planning program is said to be working well. For the first time the ever-rising enrollment in elementary schools has been checked. Much more work remains to be done, however, for even now the annual figure for abortions is said to number more than one million. The present improvement was achieved by a corps of about 32,000 persons, mostly midwives and social workers, especially trained to instruct wives, as a group or individually, in the use of contraceptives. Each worker may instruct 100 such sessions in a month, but the average is 10 or 11 a month. It is one thing to become a qualified teacher and quite another to gain enough practical experience to sell the idea of family planning by sympathetic understanding and a real insight into family problems. A town of 3,000 population is allotted one instructor who is on call at all hours of the day or night. She must hold classes at least once a week for group instruction.

Not all instructions are on contraception. The instructor may be consulted by a childless wife who wishes to become pregnant. In such a case she may find a retroflexed uterus or some other abnormality requiring a specialist's help. Because these social workers receive only a nominal salary from the government they must be imbued with a sense of lofty purpose, and above all they must love the work.

UNITED KINGDOM

Death from Cancer.—The provisional death rate in England and Wales in 1959 for all forms of cancer in men was 2,261 and in women was 2,063 per million of population. These figures show a slight decrease from 1958 for men and an increase for women. The rate for men includes an increase since 1958 from 784 to 831 per million of population of deaths from cancer of the lung and bronchus and a decrease from 1,549 to 1,430 in other forms of cancer. The rate for cancer of the lung and bronchus in women increased from 119 per million in 1958 to 123 per million in 1959 and increased for other forms of cancer from 1,810 in 1958 to 1,940 in 1959. Deaths of men from cancer totaled 51,783, of which 18,181 (over 35%) were due to cancer of the lung and bronchus. Of a total of 45,333 deaths of women from cancer, only 2,882 (just over 6%) were ascribed to this cause.

Corticotropin, Corticosteroids, and Gastric Secretion.—The first issue of *Gut* contains two papers on the effects of corticotropin and corticosteroids on gastric secretion. In one of these G. P. Crean reported on the measurement of gastric acid secretion in terms of maximal histamine secretion in 18 patients during prolonged treatment with corticotropin and corticosteroids. The amount of gastric acid secretion was suppressed in four, unchanged in three, and increased in five patients treated with corticotropin. The secretory changes ranged from complete suppression (in a patient with initially low secretion) to an increased secretion four times that in the controls. In each of the five patients treated with cortisone, and in one treated with prednisolone, secretion was increased, the increases ranging from 33 to 160% of the control level. The effects of single intravenous injections, of continuous intravenous infusions of hydrocortisone, and of intravenous infusions of corticotropin on the hydrogen ion and electrolyte content of basal and maximally stimulated secretion were also studied. In these experiments the greatest changes were seen in those patients in whom acid secretion had been noted to increase during prolonged steroid therapy.

Royal Jelly.—There is no evidence, either theoretical or from published practical tests, that any of the existing preparations of royal jelly produce any effect other than that which can be achieved easily with any other expensive material which the customer believes will do him good. Royal jelly can, therefore, be added to the long list of "magic" substances which, since the beginning of history, human beings have persuaded themselves will make them younger, healthier, and more beautiful. Such is the conclusion reached by Consumers' Association Ltd., and published in the March issue of the monthly journal, *Which?*. The main constituents of royal jelly are water, protein, carbohydrate, and fat; there are small quantities of thiamine, riboflavin, nicotinic acid, pantothenic acid, and biotin.

Expired-Air Resuscitation.—As the result of an investigation of mouth-to-airway expired-air resuscitation in 22 anesthetized paralyzed patients, J. Cox and co-workers (*Lancet* 1:727, 1960) concluded that this is an effective method of resuscitation. The patients' lungs were ventilated by expired air for periods varying from 15 to 115 minutes. Eight donors were used, none of whom had performed expired-air resuscitation previously, and in no instance was difficulty experienced in inserting the airway and starting resuscitation. The mouth-to-airway method was used, rather than the direct mouth-to-mouth method, and it is considered the method of choice as the esthetic objections to mouth-to-mouth methods are many. Great difficulty was encountered at first in maintaining an adequate mouthseal. In the end, the most satisfactory seal was found to consist of an oval soft rubber sheet with foam plastic glued to one surface. The foam plastic formed an airtight joint between the patient's face and the rubber. The conclusion reached was that mouth-to-airway expired-air resuscitation is an effective method and that it should take its place as an alternative to the standard methods, to which it is in some cases to be preferred.

Economics of Health Services.—In the April issue of *Lloyds Bank Review*, D. S. Lees pointed out that between 1949 and 1958 health expenditure, while rising dramatically in terms of money, increased in real terms by no more than 18%. This was about the same as the rate for consumer expenditure in general and much less than for welfare services. He contended that it would be difficult to maintain that the introduction of the National Health Service has resulted in a spending spree. Compared with the increase in 1938 the per capita increase in real terms was only 10%.

Had people been left to make their own choice, they might have spent more rather than less on health services. Nevertheless, the switch from private to public expenditure means, among other things, that the level of taxation is higher than it otherwise would have been by more than 1.4 billion dollars. With this sum sales taxes could have been abolished or the standard rate of income tax reduced by 28 cents. It could be maintained that, if taxation had been so much lower, greater incentives to work, save, and take risks would have raised national income above its present level and so enabled the public to enjoy the present standard of health services and to have additional funds for other uses.

An important part of the case for a national health service has been that the expenditure involved would be more than justified by the consequent increase in national output. This was true in the 19th century but has ceased to be so now that health expenditures mainly tend to add to the number of retired people in the population and to the number of women over 45 years of age. The vast majority of the population today is in good health as much through good luck and good food as through good medicine. It is doubtful whether further improvement would be an aid to output. We are thus faced with the choice between devoting resources to health or devoting them to such wealth-producing activity as education or capital investments in industry.

Death from Chewing Gum.—Two deaths due to aspiration of chewing gum into the bronchi were reported by Stallybrass and Child (*Brit. M. J.* 1:1113, 1960). A man aged 62 years, who enjoyed reasonably good health, was found by his wife, dead in his garden. At autopsy a single wad of chewing gum was found occluding the right main bronchus. Although the left ventricle was hypertrophied and both coronary arteries showed advanced calcified atheroma, there was no evidence of occlusion or of old or recent myocardial infarcts. Death was attributed to vagal inhibition resulting from sudden impaction of the chewing gum in the bronchus. Another man, aged 62 years, suddenly collapsed at work. When medical aid arrived he was found to be dead. At autopsy a wad of chewing gum was found in the left main bronchus. The main bronchus was not totally occluded, and the mucosa was inflamed. A little mucopus was present. The lungs were congested but showed no evidence of infection or collapse. The coronary arteries showed severe calcifying atheroma, but there was no thrombosis. The purulent bronchitis was taken to indicate that the chewing gum had been inhaled some time before death and that death was due to coronary insufficiency and bronchospasm. The authors have been unable to find any report of similar cases.

Mental Hospital's Social Club.—What is believed to be the first social club of its kind in this country was opened at a mental hospital in Nottingham. Known as "The Gateway," it will be run for the patients by the patients. It is housed in a modern building with a hall equipped with stage and dressing-rooms, lounge, art room, music room, tea bar, committee room, and a shop. The center cost $70,000 to build and will be run by a committee of eight: two patients from each ward of the 120-bed hospital.

Strontium-90 in Milk.—According to the second report of the Radiobiological Research Laboratory of the Agricultural Research Council, the average amount of strontium-90 in milk increased by about 40% between December, 1958, and June, 1959. The report confirmed the belief that the level of strontium-90 in milk is determined mainly by the rate of fall-out in the immediate past and not by the cumulative total in the soil. As the rate of fall-out is now decreasing, it was concluded that no further increases in the level of strontium-90 in milk are to be expected if nuclear weapons tests are not resumed.

Health Service Failings.—In a study sponsored by the Nuffield Provincial Hospitals Trust, Britain's 21,000 family doctors were charged with failure in their role of coordinators of the different services for treatment and care of the sick. The report, by Mr. Gordon Forsyth and Dr. Robert F. L. Logan, concluded that there was a risk of building too many hospitals. The 250 beds per 100,000 population found to be needed in Barrow for acute illness was only one-half the number that the hospital planners had thought necessary at the start of the National Health Service. The investigators found that not all hospital admissions were clinically necessary. If allowances were made for this, the need for beds decreased to 230 per 100,000. Fewer beds would be needed if better outpatient clinics, more home nursing facilities, better standards of housing, and willingness by the general practitioner to undertake home care were provided. The last point is crucial to the whole situation.

Under the National Health Service (NHS) the general practitioner is supposed to coordinate all the services provided. He has a unique opportunity of diagnosing before symptoms appear, when early treatment could be lifesaving. The need for early diagnosis has been accentuated by the emergence of new drugs and healing techniques. Until recently it was of only academic interest to diagnose meningitis, cancer, thrombosis, deafness, or melancholia. "It is all very well in theory to cast the general practitioner as the leader of the new advances in preventive medicine. But has he the necessary skill to take up the challenge? The death rate from coronary thrombosis in middle-aged men, with anticoagulants available, suggests that he has not."

About 20% of diabetics are undiagnosed and untreated until they present complications. The average duration of hospital stay, the investigators said, is much longer in British than in North American hospitals. One reason is the general practitioner's failure to integrate the hospital and home services. "The way in which the health service has developed in relation to general practice does not present an *encouraging* picture. If there is really to be a renaissance of general practice, instead of merely lip-service to the general practitioner, then efforts must be made to bring the general practitioner back to the hospital, perhaps with an extension of clinical assistant posts, accompanied by modifications in the method and incentives of remuneration."

CORRESPONDENCE

DERMABRASION

To the Editor:—Deep abrasion, under any of its several pseudonyms, and multiple excisions have emerged since World War II as a pair of related modalities offering great help for most patients disfigured by acne pitting. Dr. Preston C. Iverson, who popularized both techniques in the middle of the 1940's, agrees with me that effective mass use has been set back 10 years by disrepute resulting from unfortunate and highly inaccurate publicity, not entirely confined to lay periodicals. The special report by Rattner and Lazar in The Journal, Dec. 26, 1959, page 2326, helps to correct some of the false implications regarding the degree of perfection and the universality of satisfactory results to be anticipated, but it fails to emphasize the following essential points.

For the more hideous deformities of this type, use of painstaking multiple excisions (often hundreds in several stages) is the more important of the two related techniques and is largely responsible for most of the better results. Such excisions are not compatible with superficial local anesthesia as described in the recent article.

Improvement of appearance by abrasion is primarily related to normal viewing distances and lighting conditions. Saucerization tends to reduce the intensity of shadows cast in the center of deeper pits, a change rarely noticeable on close inspection under the harsh lighting of bathroom mirrors.

Among surgeons with the longest experience in abrasive therapy, prognosis for any single patient is still deemed all but impossible. Wide variability in results does not seem to be well explained by classification of types. Furthermore, results should not be judged within the first few weeks. As skin completes the regeneration process, many pits tend to reappear or again become more prominent.

In spite of the uncertainties and drawbacks, reasonable improvement attained in the average patient makes these procedures ones which I would unhesitatingly elect for myself or my family.

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To the Editor:—The article in The Journal by Rattner and Lazar fails to give credit to Dr. Preston C. Iverson of Philadelphia for originating the method of dermabrasion. In his original paper, "Surgical Removal of Traumatic Tattoos of the Face," (*Plast. & Reconstruct. Surg.* 2:427-432 [Sept.] 1947) he calls attention to the use of dermabrasion for the elimination of traumatic tattoos which he encountered as a surgeon working in army hospitals during World War II. In a second paper, "Further Developments in the Treatment of Skin Lesions by Surgical Abrasion," published in the same journal (12:27), he described the application of this technique to many other facial disfigurements. Iverson's second paper was published in July, 1953, and Kurtin's in October, 1953 (*A. M. A. Arch. Dermat. & Syph.* 68:389).

From the paper by Rattner and Lazar one gets the impression that Kurtin was the first to report on the method of dermabrasion. Credit should be given to Kurtin for improving on the method by using a rapidly rotating brush and freezing the skin with ethyl chloride, but the fundamental concepts of dermabrasion should be credited to Iverson's original contribution. It is difficult for any author to be familiar with all sources of progress in medicine, but in a review article such as this it seems inexcusable to fail to acknowledge that the original concept of abrasion was made by Iverson, a plastic surgeon, and only modified by Kurtin, a dermatologist. I have heard verbally from my colleague, Dr. V. H. Kazanjian of Boston, that he had used the method even before Iverson's publication but that he did not report it in the surgical literature.

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To the Editor:—Take a look at the "before" and "after" pictures in the special article on dermabrasion. Any of the illustrations would demonstrate my point, but look particularly at figure 4. The "before" picture is taken with a light directed from above and to the side to show a maximum of the texture of the deformities in the skin. The "after" picture is taken with the light straight ahead in front of the patient to show the minimum of texture of the scars. The "before" picture is taken close to the patient, thereby showing the scarring to the maximum. The "after" picture is taken farther away, thereby minimizing the scarring. Note the blackness of the hair at the temples on the before picture and its contrast with the dark grayness of the temple hair on the after picture. This suggests that different films were used or the processing of the pictures was altered to make the scarring more prominent in the "before" picture and less prominent in the "after" picture.

There are few photographic devices that could have been used to make these pictures more misleading. If the authors of this article were duped by a professional photographer who wanted to please them by making their results look good by trick photography, I feel sorry for them instead of angry. But this is scientific dishonesty, and most readers of The Journal will not be aware of the trickery. The authors and the editors have slipped.

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The above comments were referred to the authors of the article, and they have submitted the following reply.

To the Editor:—The assignment undertaken by Dr. Lazar and me was to discuss dermabrasion for the improvement of acne scars in the light of our experience with the method. We were not asked to write a review article. While it may not be technically correct, usage has decreed that the term "dermabrasion" refers to the method introduced by Kurtin. Accordingly, we did not think it necessary to review the literature thoroughly. We referred only to specific articles mentioned in the paper. Also, on page 2328 we made the following statement. "It *was evident at once that the method was unquestionably* the best one yet devised for the treatment of acne scars. In the past, numerous measures had been tried, including scarification, electrodesiccation, surgical excision, surgical shaving, chemical caustics, cryoslush therapy, and the widely publicized abrasion with sandpaper, but all procedures had been found wanting." Dr. Cannon's and Dr. DeKleine's points are well taken; we believe, however, that they embrace a larger subject.

I asked the photographer to comment on the specific points raised in Dr. Truman's letter. He assured me that the film, paper, and processing are always the same but that in order to picture the scars accurately, it is necessary to alter lighting, before and after, and sometimes even to change slightly the position of the head. A change in hair style is not important as long as the lens centers on the scars. He is prepared to support these views before any body of experts. As to the point that was raised in regard to figure 2, he tells me that the lighting was identical but that some detail was lost in the reproduction. These comments were then firmly supported by a production executive in the medical book publishing field who is an expert on the subject, and after making a careful examination he also attested to the authenticity of the photographs.

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To the Editor:—A review of the literature on dermabrasion shows that Kromayer, in 1905, published an account of use of a motor-powered instrument to improve scars and other disfigurements of the skin. He also noted that ethyl chloride could be used as an anesthetic and skin hardener. In 1929 Kromayer first mentioned a leveling operation for smallpox scars, and in 1933 he published another paper on abrasion with steel burs, which he used for superficial conditions such as juvenile warts, freckles, and pigmentations. In 1947 Iverson reported on his use of carpenters' sandpaper, grit 0-00, wrapped around a 3-in. (7-cm.) roll of gauze bandage. He successfully removed traumatic tattoos from the faces of patients under general anesthesia. In 1948 McEvitt applied the use of sandpaper to treat postacne scarring. In 1952 Kurtin introduced his method of corrective surgical planing of the skin. The abrasion was performed with motor-driven steel brushes, and ethyl chloride was used as a local anesthetic and skin hardener. The use of ethyl chloride provided a rigid bloodless field for abrasion which helped make this method adaptable as an office procedure. After Kurtin's report medical interest in dermabrasion was stimulated, so that at present it is a widely used procedure.

V. L. Conley, Ph.D.
Secretary
A. M. A. Committee on Cosmetics

URINARY CONTROL

To the Editor:—In his splendid article, "Development of Urinary Control in Children," which appeared in The Journal, March 19, page 1256, Dr. Muellner states, "Man's ability to void at any degree of bladder filling is a unique biological phenomenon which no other mammal manifests. An apparent exception is the male dog (and other canines), who is able to deposit small amounts of urine at each pillar and post."

I have two female Dalmatians, mother and daughter, aged 10½ and 7½ years, who show the same characteristic to a marked degree. Possibly the fact that they have both been spayed has something to do with this phenomenon. Often they will deposit small amounts of urine in as many as a dozen places within a few minutes, usually in places which have recently been used by male dogs. This would tend to confirm Dr. Muellner's statement that this act "is more closely related to the sex drive than to the ordinary function of micturition." On many occasions, when I take them both out, the mother dog will wait patiently until her daughter has finished voiding and will then proceed to void on the same spot; the reverse never happens.

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FOREIGN MEDICAL GRADUATES

To the Editor:—The letter from Henry S. Gupta in The Journal, March 19, page 1321, points up the lack of uniformity in the requirements of the specialty boards in the United States. Dr. Gupta implies that foreign doctors are discriminated against by all the specialty boards, regardless of whether or not they have graduated from a fully approved medical school in their own country and have completed the required course of approved residency training in America. This is not the case. Several of the specialty boards, including those for surgery and pathology, admit to examination physicians from foreign countries who are still citizens of their own country. On the other hand, a certain few of the boards do not, including those for obstetrics and gynecology, dermatology, internal medicine, and orthopedic surgery.

As Dr. Gupta points out, many physicians who are citizens of foreign countries and who come to this country for postgraduate training do so to equip themselves to return to their native land better qualified to practice good medicine. It would appear that we should do all in our power to facilitate the training of foreign physicians coming to our shores, in the interest of better medical care the world over; improved hygiene, especially in the backward countries; and closer fellowship with medical colleagues on every continent. Properly trained, it is but natural they should desire the prestige afforded from certification by a specialty board. It is time our specialty boards established more uniform requirements for certification.

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FOREIGN SCHOOLED INTERNS

To the Editor:—As a foreign graduate I was interested in your recent editorial on the problem of the foreign-trained intern (*J. A. M. A.* 172:1048 [March 5] 1960). From personal experience, I am able to confirm the fact that certain hospitals look on the foreign graduate as a source of cheap labor to be exploited for examining patients without consideration to furthering their medical education or skills.

Some remarks in your otherwise excellent editorial are presumptuous. Most medical graduates have been used to adequate food and middle-class surroundings. For a sophisticated, educated person there is little to admire in most of American television, and American movies are available the world over. The food I received in the internship, which I left in short order, was as low in quality as any I had eaten in England during the worst part of the war. Furthermore, a foreign intern has little opportunity to enjoy the high standards of living of America except as a spectator when stipends are so small.

Another problem is the concentration of foreign interns in nonteaching hospitals. Most of these hospitals pay a higher stipend than do the teaching hospitals, and as foreign graduates are totally dependent on their stipend, having no family or other means of supplementing it, such as working wives, they gravitate toward higher paying institutions.

Although the problem is not simple, it can be solved. I left a poorly run internship, in which I was exploited, for a superior, well-supervised, well-taught internship in Ohio in a nonteaching hospital. Such an internship requires the will and cooperation of the entire medical staff and, most important, the administration.

The state licensing boards also have a part to play. If a physician cannot be licensed in the state in which he is doing his internship, he naturally feels resentful. He is considered responsible and trained well enough to treat many types of emergencies and seriously ill persons, often with little supervision, while working in an exploitative situation, but he cannot be trusted to the independent practice of medicine with reasonable rewards.

There are good hospitals that are not affiliated with teaching hospitals which give the foreign graduate an excellent background and training. Those hospitals that do not live up to the standards required should be disapproved for all intern training under both the matching plan and the State Department's exchange visitor program. I believe that the State Department has been too lax in approving poorly run programs under the exchange visitor program. By raising the standards required citizens of the United States would give a far better impression of the United States and its medicine to the foreign graduate, both to the one who remains and the one who returns to his home land; also, better patient care would be insured.

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HOME VISITS TO INVALID PATIENTS

To the Editor:—In the article, "The Psychotherapy of Paralysis Agitans," by Doshay, in The Journal, March 26, page 1347, I was moved by the report of the invalid woman who had to be dragged to the psychiatrist's office every two months until her sick husband finally died from the strain of these efforts. The conclusion drawn was that better community facilities would have prevented this tragedy. I must admit that while my practice was confined to institutional work I too had tubular vision which allowed me to see only a limited spectrum of solutions to problems of this sort. I am familiar with the geography of New York City, and I know that the route from Presbyterian Hospital to Staten

Island is a direct one and has only a ferry and a few traffic lights as hindrances. I am sure that a more direct approach to this patient's problems would have preserved her husband's life; a car trip could have been made by the psychiatrist to the patient's home once every two months. This is a most reasonable suggestion because these infrequent visits obviously were not for physiotherapy.

We should deplore the current trend of some specialists to refuse home visits even when they know that the patient cannot travel without great difficulty. I cannot understand how a physician who is aware of these conditions can shamelessly write a report of such a case in a medical journal. I am certain that one home visit to this patient would have given the psychiatrist more insight into her problems than a dozen interviews obtained just after she was dragged from house to car and from car to office. I hope my letter will help move some specialists from the desk where they write sad laments to the bedside where they can do some good.

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TREATMENT OF MALIGNANT PLEURAL EFFUSION

To the Editor:—"Treatment of Malignant Pleural Effusion by Talc Poudrage," by George J. Haupt and others, in The Journal, Feb. 27, page 918, has caught my attention. I believe that the procedure described is absolutely unnecessary. We now have such adequate chemotherapeutic agents as nitrogen mustard or thio-TEPA which will accomplish the same purpose more effectively. In addition, repeated injections of these drugs will cause far less morbidity and give much better results than any method involving thoracotomy.

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The above comment was referred to the authors of the article cited, and they have submitted the following reply.

To the Editor:—It was because of our unsatisfactory experience with the use of colloidal radioactive gold and chemotherapeutic agents that we adopted the procedure of talc poudrage. In our hands, recurrent pleural effusions due to malignant pleural tumors by repeated thoracentesis and installation of chemotherapeutic agents were eliminated in only about 50% of the patients. On the other hand, as we reported in our article, we have never failed to eliminate such effusions by talc poudrage.

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LATINONIAN EXCHANGE

To the Editor:—This is to express my admiration for Dr. Foraker's skillfully written satire, "Latinonian Exchange," which unfortunately was rather buried on page 168 of The Journal, Feb. 27. I hope many others found it because the kind of situation it describes is all too prevalent.

Having served my clinical clerkship at Strong Memorial Hospital in Rochester in 1938 to 1939 and my internship in the Children's Medical Service at Bellevue Hospital in 1939 to 1940, I am one of those who learned medicine at its uncrowded best and with the enormous privilege of constant close personal contact with great teachers as well as top residents. The changed picture which exists today and which is so well illustrated in the biting description of Metrocolossal University can only lead to loss on all sides. On the one hand we admit our desperate need for foreign residents to man our medical services, and on the other hand we muff the opportunity to make them really useful to us and useful to their own communities when they return home.

One such pungent article will, I think, do more than 50 lectures to bring home these points. I hope you will have more such satires on some of the glaringly weak points in modern medical practice.

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ETHYL ALCOHOL LEVELS IN THE BLOOD

To the Editor:—With reference to the effects of alcohol used as an antiseptic on the alcohol content of the blood, Dr. Heise, in The Journal, March 12, page 1197, agrees with Dr. Beeman that "alcohol . . . should not be used when blood alcohol tests are made," but the reason given is that "this procedure would cause needless arguments in court." May I point out that this reason is entirely beside the point? Far more important than "needless arguments" are morality and justice.

I have found 0.2% or more alcohol in blood entirely as a result of alcohol used to sterilize the skin (*Am. J. Med. Jurisprudence* 2:261 [July] 1939; *Canad. Bar Rev.* 26:1437 [Dec.] 1948). The question of whether the alcohol entered into the blood because the syringe had been rinsed with alcohol to withdraw the blood or for some other reason is of purely academic interest. The important objection to alcohol as an antiseptic is not that it may cause needless arguments but that innocent persons may be convicted because of false blood alcohol values.

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ABSTRACTS FROM THE LITERATURE

INTERNAL MEDICINE

Critical Study of Flocculation Tests: Their Replacement by Sandor's Reticuloendothelial Diagram. E. Aron and R. Vargues. Presse méd. 68:103-104 (Jan. 23) 1960 (In French) [Paris].

Sandor's reticuloendothelial diagram (SRD) is described and compared with several hepatic flocculation tests usually applied for diagnostic purposes. The flocculation tests attempt to determine the quantitative changes in some serum proteins with the use of several artificial means of precipitation, while the SRD, obtained by varying the pH, gives an accurate picture of the serum globulin balance without modifying the blood proteins or changing their nature. Sandor's technique consists in precipitating the globulins by successive additions of a buffer solution, and determining the optical densities with a photometer. In normal serums the gamma-globulins precipitate at pH value of 6.5 to 7.5, and the alpha-globulins, at 4.5 to 5.5. When the pH is 7.5, the quantity of insoluble globulins is minimal (0.50 Gm. per liter). If this quantity is higher, as is the case in cirrhosis and hepatitis, the gamma-globulin precipitate is measurable. Ponderal analysis of the precipitating globulins at a 7.5 pH led to the conclusion that the concentration of gamma-globulins must be higher than 1 Gm. per liter to give a precipitate which can be detected by opacimetric methods. Thus, the increase or decrease in precipitation in the alkaline zone corresponds to either a hypergammaglobulinemia or a hypogammaglobulinemia.

The SRD, as adjusted for clinical application, gives an accurate quantitative and qualitative distribution of insoluble globulins. In normal serums the curve is always the same. In icterogenic hepatitis there is a significant and simultaneous increase in beta-globulins and gamma-globulins. In obstructive jaundice there is a hyperbetaglobulinemia, sometimes with a slight hyperalphaglobulinemia. In liver cirrhosis there is a typical diagram which at the same time stresses the fall in alpha-globulins and a moderate increase in gamma-globulins. Although they confirm these findings in a general way, the flocculation tests distort and magnify the changes in the serum globulin picture as a result of the artificial devices used. The SRD, because of its precision and simplicity, should replace the flocculation tests in hepatology.

The Epidemiology of Primary Atypical Pneumonia. H. B. Harding and R. A. Snyder. A. M. A. Arch. Int. Med. 105:217-232 (Feb.) 1960 [Chicago].

The authors report on an explosive outbreak of a severe respiratory infection at Northwestern University in Evanston, Ill. Nineteen persons became ill with the disease in a period of 22 days. Fever accompanied by headache, malaise, and generalized aching occurred within a 4-day period in 14 of these persons, followed by secondary cases in 5 persons over an interval of 5 days. Within 2 or 3 days cough, which varied in productivity, developed. Physical findings in the chest were at variance with the chest roentgenograms. Of 14 persons with marked x-ray lesions, 5 showed only slight physical signs of pneumonitis. Two other patients with no abnormal shadows on chest roentgenograms showed marked physical evidence of pneumonitis. A thorough study of this outbreak was made with the aid of bacteriological, virological, and serologic methods. The outbreak was classified as primary atypical pneumonia, because the symptoms were typical, the chest roentgenograms of 14 of the patients were characteristic, and cold agglutinin studies yielded positive results from specimens of 8 of the 10 patients tested. Negative virus complement-fixation studies further supported the diagnosis.

The study of this outbreak led to an investigation of 96 sporadic cases of primary atypical pneumonia in patients who came to some of Northwestern University medical school's affiliated hospitals and clinics between January, 1953, and March, 1957. In these patients the cold agglutinin test proved to be a more successful method of demonstrating serologic evidence of this disease than did the agglutinin test for Streptococcus MG organisms. The sporadic type of the disease was observed more often in the late summer and fall than at other times of the year, and more often in women than in men. Of the 96 patients, 21 were treated with penicillin, 19 with chlortetracycline (Aureomycin), and 21 with oxytetracycline (Terramycin); the remaining 35 patients were treated with various combinations of penicillin, chloramphenicol, streptomycin, erythromycin, oxytetracycline, tetracycline, and Mysteclin (a combined preparation of tetra-

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The place of publication of the periodical appears in brackets preceding each abstract.

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cycline and nystatin). Treatment with the broad-spectrum antibiotics was followed by a rather prompt drop in fever, but the total time of illness, as determined by chest roentgenogram evidence of disease, was not significantly altered.

Evidence for the possible existence of a subclinical type of the disease has also been presented. It again has been found that primary atypical pneumonia apparently is not due to any of the common bacteria or to the better known viruses or rickettsias. The literature concerning the disease has been extensively reviewed, including the techniques for, and the mechanism of, the cold agglutinin and Streptococcus MG agglutinin tests.

Diabetes Mellitus and Carcinoma of the Pancreas.

B. Lemass. Irish J. M. Sc. 6:16-34 (Jan.) 1960 [Dublin].

The author observed a patient with a strong family history of diabetes mellitus, in whom the classical symptoms of diabetes mellitus developed, and who then suddenly had obstructive jaundice. At laparotomy it was found that there was a small carcinoma localized at the head of the pancreas and obstructing the common bile duct. The patient survived a partial pancreatectomy for 5 years. This case raised some questions in the author's mind regarding the character and behavior of diabetes mellitus as a manifestation of pancreatic tumor. He reviewed the records of 66 patients with pancreatic carcinoma seen at the Royal Victoria Hospital, Montreal, over the period 1944-1954. Of the 66 patients, 18 (27%) showed glycosuria, and 20 had blood sugar levels in the diabetic range. The curves plotted on the basis of sugar tolerance tests were reduced in 10 patients, and in 8 they were of diabetic character. Contrary to expectations, only 3 patients gave a positive family history of diabetes, and in only 1 of these did diabetes develop in association with the carcinoma.

Malignant disease of the pancreas predominantly affects men (M:F = 2:1). Consequently, when diabetes develops in a male patient over 40 years of age, a possible underlying tumor should be thought of, especially if the man has gastrointestinal symptoms or back pains which cannot be fully explained and which fail to clear up when the diabetes has been brought under control. Classical diabetic symptoms were noted in only 7 cases in this series. Diabetes was recognized before the tumor in 6 cases, and in 3 of these it preceded all other manifestations of the tumor by intervals of 1, 7, and 12 months respectively.

Gross examination of the pancreas at autopsy revealed that among 30 patients, in whom the tumor was confined to the head of the pancreas, there were 7 who had diabetes. None of the tumors confined to the tail of the pancreas was associated with diabetes, despite the high concentration of islet tissue in the tail. The presence of diabetes in a patient suspected of having pancreatic tumor need not always mean that the gland is extensively destroyed by the tumor and, therefore, hopeless. In the author's case-material there were a number of diabetic patients in whom gross and microscopic examination of the pancreas at autopsy failed to reveal extensive islet destruction, and in a few cases the tumor was clearly small and localized when the carbohydrate tolerance was known to be impaired. In short, there seemed to be much variability in the extent and nature of the lesion that may result in the diabetic state.

Fourteen of the 20 diabetic patients required insulin, and the doses had to be increased as the tumor progressed. Although in 10 of the patients requiring insulin an average of 26 units per day was adequate, the others were relatively resistant to it, and their sugar metabolism was poorly controlled by large doses of insulin.

Asymptomatic Bacilluria in 68 Diabetic Patients.

R. T. Rengarts. Am. J. M. Sc. 239:159-164 (Feb.) 1960 [Philadelphia].

The author had observed that not infrequently diabetic patients entering hospital are found to have positive urine cultures despite lack of symptoms of urinary tract infection. Furthermore, after appropriate treatment for the asymptomatic bacilluria, considerable decrease in the daily requirement of insulin often occurs. These findings suggested that the bacilluria might be of importance clinically, and the question arose as to what features characterize the diabetic who enters hospital with asymptomatic bacilluria.

All diabetic patients admitted to one section of the Joslin clinic service of the New England Deaconess Hospital, Boston, submitted "clean" voided specimens of urine for culture, colony count, sensitivity studies, and determination of sugar content. Male patients submitted midstream clean voided specimens. Females were cleansed with tincture of benzalkonium (Zephiran) chloride, 1:1000, and specimens were collected in a sterile container. Samples from specimens were incubated within one hour after voiding. Among the 68 patients (22 males and 46 females) without urinary tract disease, 23 (34%) were found to have asymptomatic bacilluria with colony counts greater than 100,000 per milliliter of urine. Sixty-eight per cent of the patients confined to bed prior to entry had bacilluria to this extent, as compared with 14% of the patients not confined to bed prior to hospital admission. Findings in the urinary sediment were of little value in indicating those patients with asymptomatic bacilluria of significant degree. The sugar content of the urine showed no consistent correlation with the frequency of bacilluria or the number of organisms cultured. Organisms causing bacilluria to the extent of 100,000 per milliliter of urine, or greater, were most frequently Escherichia coli, Staphylococcus albus, and Proteus and Aerobacter organisms.

Bacilluria with a colony count greater than 100,000 per milliliter of urine was present in 41% of females and 18% of males. Asymptomatic bacilluria was definitely more common in diabetic patients who had been confined to bed prior to admission than in those who had been ambulatory. The author concludes that, among diabetic patients entering hospital for various reasons, there is a significant percentage with asymptomatic bacilluria despite the absence of symptoms referable to urinary tract infection. Only by routine cultures and colony count carried out with a "clean" voided specimen of urine can such bacilluria be found.

Some Cases of Paraproteinemia Illuminated by Immune Electrophoretic Findings. J. Clausen and A. Videbaek. Ugesk. laeger 122:103-107 (Jan. 28) 1960 (In Danish) [Copenhagen].

In 3 cases of paraproteinemia immune electrophoretic diagnosis was made of gamma myeloma without Bence-Jones protein, beta-2-A myeloma with Bence-Jones protein, and Waldenström's macroglobulinemia with abnormal aggregates in the serum. In all cases the immune globulins, beta-2-A globulin, beta-2-M globulin, and gamma globulin, were affected; the paraprotein in the cases of myelomatosis was immunologically of either gamma globulin or beta-2-A globulin type, and in Waldenström's macroglobulinemia the paraprotein was of beta-2-M type. In all cases there was a hypoimmunoglobulinemia, which explains the lowered resistance to infection in 2 patients. In one case Bence-Jones protein was found in the serum. Serum from the patient with Waldenström's macroglobulinemia showed an increase in beta-2-M with depression of the other 2 immunoglobulins. Paper electrophoresis affords excellent help in most cases of paraproteinemia, but immune electrophoresis is an extraordinarily useful adjunct in the further classification and study of these conditions and particularly in the not infrequent atypical cases of paraproteinemia.

South American Blastomycosis Associated with Hodgkin's Disease. D. L. Altério and G. del Negro. Hospital 57:73-80 (Jan.) 1960 (In Portuguese) [Rio de Janeiro].

The association of deep mycosis with malignant lymphoma or reticuloendotheliosis seems to be more than simple coincidence. The authors report a case demonstrating the combination of South American blastomycosis with malignant lymphogranulomatosis (Hodgkin's disease), which they believe to be the 2nd reported in medical literature. The patient, a 49-year-old man, was admitted to the Hospital das Clínicas, University of São Paulo, because of persistent cough, anorexia, loss of weight, and a daily temperature that varied between 39 and 40 C (102.2 and 104 F). The patient had a history of ulceration of the mouth and pharynx, for which he had been treated, and from which he had recovered 15 years before his admission to the hospital. Direct examination of the sputum for Paracoccidioides brasiliensis showed a positive result, and therapy with sulfanilamide derivatives was instituted. There was some improvement as to the patient's temperature and appetite. After 10 days of treatment the administration of sulfanalamides had to be interrupted because of toxic reaction. The patient left the hospital and continued under observation as an outpatient. At the end of 4 months of unsuccessful chemotherapy, a treatment with antiblastomycotic vaccine was instituted, a dosage of 1 cc. being injected intramuscularly every 4 days, plus administration of 2 tablets of sulphafurazole every 6 hours. Again no improvement was observed.

Physical examination revealed 2 important changes—mild splenomegaly and moderate generalized adenopathy. At the same time a biopsy specimen from the axillary lymph nodes showed evidence of malignant lymphogranulomatosis. Therapy with triethylene melamine was instituted and brought the patient a short remission of symptoms. His condition was still unsatisfactory when this article was written.

The authors believe that Hodgkin's disease developed in this patient while he was suffering from South American blastomycosis. It is pointed out that the association of mycosis and reticuloendotheliosis is a problem yet unsolved, but that a possible explanation is the involvement of lymph nodes in the course of mycosis, resulting in transitional histopathological and clinical aspects. Thus, the complex clinical picture appearing in the course of one condition, blastomycosis, may simulate another, reticuloendotheliosis.

Two Cases of Strongyloides Stercoralis Diagnosed by Duodenal Intubation. T. H. Celsi and A. B. Trevisan. Prensa méd. argent. 46:2289-2292 (Sept.) 1959 (In Spanish) [Buenos Aires].

The authors report on 2 patients in whom duodenal intubation revealed the presence of larvae of Strongyloides stercoralis. The 1st patient, a 28-year-old woman, was admitted to hospital because of epigastric pain, heartburn and vomiting. The patient had a history of gastrointestinal and nervous disorders, but physical examination, roentgenographic study, and laboratory tests showed no evidence of peptic ulceration. The finding of S. stercoralis larvae by duodenal intubation led to therapy with antihelminthic preparations, which resulted in clinical and subjective improvement. Subsequent intubations were negative, and the patient was discharged in good general condition. The 2nd patient, a 26-year-old woman, was admitted to hospital with partial obstructive jaundice and symptoms of lithiasis. Cholecystography was negative for lithiasis, and duodenal intubation yielded S. stercoralis larvae. Specific clinical treatment of the jaundice and antihelminthic therapy resulted in complete recovery. The authors believe that duodenal intubation is the most adequate method for investigation of S. sterocoralis, a parasite that causes constant eosinophilia; its presence may result in acute conditions with diarrhea and duodenitis, which in turn may be an etiological element in obstructive jaundice.

Cardiac Rupture Complicating Myocardial Infarction in the Aged. F. D. Zeman and M. Rodstein. A. M. A. Arch. Int. Med. 105:431-443 (March) 1960 [Chicago].

Of 365 women and 303 men who died at the Home for Aged and Infirm Hebrews of New York between 1942 and 1955, and on whom autopsies were performed, acute myocardial infarction was observed in 44 women and 37 men. Among these 81 patients there were 16 cases of cardiac rupture, 15 through the ventricular wall and 1 through the base of the posterior papillary muscle; 4 of the patients were men and 11 were women. Cardiac rupture did not occur in the remaining 65 patients. The clinical and autopsy records of the 15 patients with cardiac rupture through the left ventricular wall were compared with those of 62 patients without cardiac rupture. The incidence of 2.4% of cardiac rupture in the entire series, and of 19.75% among the patients with myocardial infarction, is among the highest reported in the literature. The average age of 80 years of the patients with rupture makes it the oldest series yet reported. The average age of 78 years of the patients without rupture is also worthy of note.

The clinical and pathological findings in the patients with rupture of the heart differed from those reported by other observers in patients less advanced in years in the following respects. The patients in this series showed a greatly increased incidence of the condition itself, a greater preponderance of women, and less marked correlation with undue exertion after infarction, as well as more examples of preceding heart failure and of mental impairment. The high incidence of rupture in the patients of advanced age, attributed by other observers primarily to the increased incidence of acute myocardial infarction in aged women, was strikingly confirmed by this group of patients of advanced age. Aged women with acute infarction are particularly susceptible to cardiac rupture, since, with a retarded age of onset of coronary artery disease, they lack the protective effects provided by the increased collateral circulation, the myocardial fibrosis, and the muscular hypertrophy which develop with long-standing coronary artery disease. The increasing number of women living to advanced age is a significant factor in the high incidence of cardiac rupture in the aged.

The diagnosis of acute myocardial infarction in older persons is made more difficult, or often missed completely, in the absence of autopsies because of the frequent presence of complications or overshadowing associated diseases and because of the impaired sensitivity to pain secondary to changes in the sensorium. The necessity for a high index of suspicion of myocardial rupture as a complication of infarction in the aged is emphasized. The need for careful conservative treatment of infarction in the aged is discussed, with particular reference to the need for strictly limited activities and sedation, as well as for caution in the use of vasopressor drugs in the treatment of shock. In view of the suspicion that anticoagulant therapy may contribute to the occurrence of cardiac rupture, it is noteworthy that none of the patients in this report were given such treatment. The suggestion is made that all mortality studies of myocardial infarction attempting to evaluate the effect of anticoagulant therapy should include data concerning the age and sex of the patients.

Simultaneous Tachycardias. A. Castellanos Jr., L. Azan, and J. M. Calviño. Am. Heart J. 59:358-373 (March) 1960 [St. Louis].

Various combinations of simultaneous tachycardias have been observed to occur in the human heart. The coexisting atrial and ventricular forms are the most frequent. When esophageal leads were used, the incidence of these arrhythmias was found to be greater than that reported by other authors. This greater incidence was due to the fact that without esophageal leads the atrial rhythm in many cases could not be interpreted correctly because the widened QRS complexes sometimes obscured the atrial deflections. Digitalis was the cause of these arrhythmias in over 75% of the cases studied. This was well demonstrated in cases in which the double rhythms were induced by the intravenous administration of short-acting digitalis preparations. Appropriate treatment with potassium and procaine amide usually abolished the tachycardias promptly. Contrary to the usual belief, the prognosis was not necessarily dependent upon the nature of the disorder of the rhythm but chiefly upon the precarious conditions of the myocardium. As a rule, these arrhythmias were most frequently seen in elderly patients with arteriosclerotic heart disease. A single exception was that of simultaneous tachycardias occurring in a 9-year-old girl with rheumatic fever, who died several days after sinus rhythm was restored. Whenever the rate of the lower pacemaker was rapid enough, it was conceivable that the atrial impulses could not transverse the A-V junction because of the refractoriness provoked in the latter by the lower pacemaker. However, it was demonstrated that some degree of abnormal refractoriness or true block was present. Yet, obviously, a complete A-V block did not exist. This impedance to conduction was ascribed mainly to the toxic effects of digitalis.

The "Straight Back" Syndrome: A New Cause of Pseudoheart Disease. M. S. Rawlings. Am. J. Cardiol. 5:333-338 (March) 1960 [New York].

The author calls attention to a deformity of the chest, which he prefers to call the "straight back" syndrome. It is a congenital absence of the normal, gentle kyphotic curve of the upper thoracic spine. The condition seems to be the opposite of "funnel chest"; instead of deformity affecting the sternum, there is flattening of the upper thoracic spine. This syndrome may produce pseudoheart disease in 1 of 2 ways. First, as in funneling of the sternum, there is a decrease in the anteroposterior diameter of the chest, noticeably in the region of the upper thoracic spine. This causes false enlargement of the heart in the frontal view, particularly in the great vessel area and waist of the heart, since there is compression of these structures between the sternum anteriorly and the straightened, somewhat inwardly displaced thoracic spine posteriorly. The second means of producing pseudoheart disease seems to be by compressing or kinking the great vessels. This distortion appears to produce mechanical murmurs in systole located near the base of the heart or over the precordium.

In a period of 3 years the author was able to collect 9 cases of straight back syndrome which had been masquerading as heart disease. The degree of deformity varied from mild cases with torsion murmur and no enlargement to severe cases with actual widening of the heart shadow. The milder cases were more frequent and usually presented slightly harsh, late systolic murmurs over the base of the heart accompanied by increased pulmonic closure sounds on auscultation, and "filling" of the heart waist on x-ray examination. Fluoroscopically, this filling represented rotation and impingement of the pulmonary conus against the retrosternum in the area of the murmurs. One of the patients had been refused life insurance because of a persistent harsh systolic murmur at the base of the heart. Rheumatic fever had first been suspected, and as a result the patient spent 6 weeks at bed rest. In another patient a mistaken diagnosis of interventricular septal defect had been made. Still another patient had been refused employment because of an "enlargement" of the heart, which later was proved to be false on a lateral roentgenographic exposure. Recognition of this condition may avoid iatrogenic heart disease.

Spontaneous Perforation of the Esophagus in Hodgkin's Disease: Report of Three Cases and Literature Review. W. O. West and B. A. Bouroncle. Am. J. Gastroenterol. 33:335-342 (March) 1960 [New York].

The authors report on 2 women, aged 35 and 45 years, and on a 65-year-old man with Hodgkin's disease, who were admitted to the Ohio State University Hospital in Columbus, and in whom spontaneous perforation of the esophagus occurred. All 3 patients had a history of established generalized disease. The esophagus was the only part of the gastrointestinal tract that was involved. Dysphagia was the common symptom. This developed 4, 5, and 23 months before the diagnosis of perforation was made. A roentgen-ray examination of the esophagus was performed only in the man before the perforation. One of the women and the man had received nitrogen mustard therapy 1 and 5 months before the perforation occurred. None of these patients were subjected to esophagoscopy before the perforation. Two patients responded well to local deep roentgen-ray therapy with subsequent closure of the perforation; local deep x-ray therapy seems to be the treatment of choice.

A review of the autopsy files of the department of pathology of the Ohio State University Hospital, covering the years from 1937 to 1959, showed that the diagnosis of Hodgkin's disease was established in 170 patients. Of these, gastrointestinal involvement occurred in 26 (15.3%). The esophagus was involved in 5 (2.9%) of these patients, including 1 of the 3 patients with spontaneous perforation. Only 17 cases of esophageal involvement due to Hodgkin's disease were collected from the literature. This report brings the total to 24, and spontaneous perforation occurred in 5 of these.

Subacute Bacterial Endocarditis in Old Persons. W. J. Gleckler. Geriatrics 15:152-157 (March) 1960 [Minneapolis].

A series of 10 consecutive cases of subacute bacterial endocarditis in patients over 55 years, seen at the Community Hospital of San Mateo, Calif., were reviewed. Only 3 of the 10 patients had the clinical picture commonly associated with the disease, namely, fever, weight loss, petechiae, and other embolic phenomena, and changing heart murmurs, splenomegaly, and leukocytosis. Of the remaining 7 patients, 3 presented with psychosis, and the other 4 patients with atypical symptoms had either gastrointestinal disease, renal insufficiency, simple wasting, or apoplexy as the presenting symptom.

The chief obstacles to the diagnosis of subacute bacterial endocarditis in aged persons are the common occurrence of a variety of pathological processes of differing etiology in the same person and the difficulty in distinguishing the most significant clinical findings. The disease often seems simply to accentuate previously present pathological processes, and it is easy to assume that the accentuation is due to the advancement of the originally present processes rather than to a new disease. Thus, a slight heart murmur is easily passed off as being due to arteriosclerotic heart disease, while it may really be due to the valvulitis of rheumatic fever, and, consequently, a clinical clue to the cause of an obscure fever may be overlooked. A low-grade, evanescent fever is easily taken to indicate a "patch of bronchopneumonia."

In this series of cases a heart murmur was the only clinical feature that was present in all the patients, and the serum protein pattern always showed a reversal of the albumin-globulin ratio in the patients in whom this factor was investigated. The detection of a heart murmur in an elderly person, therefore, should be a reminder of the possible existence of bacterial endocarditis, even if the remainder of the clinical picture seems to suggest a psychosis, renal insufficiency, gastrointestinal malignancy, or other illnesses. While formerly the opinion was widely held that subacute bacterial endocarditis was strictly a disease of the young, in recent years from 10 to 50% of the cases reported in several series have been in patients over 50 years of age. This incidence is likely to increase as the proportion of our population over 50 years of age increases. The success of modern antibacterial therapy is a practical reason for attempting to improve the frequency of correct diagnosis of the disease.

The Importance of Unrestricted Diet in Treatment of Peptic Ulcer. E. A. Marshall. J. Arkansas M. Soc. 56:371-374 (March) 1960 [Fort Smith].

The author reports on 3,877 patients with peptic ulcer, confirmed by roentgenographic examination, who were seen between July, 1946, and July, 1948, and were treated by adequate antacid-sedative therapy, aluminum hydroxide being administered every 30 minutes for 16 hours a day, at bedtime, and within 2 and 4 hours after retiring, and one alkaline sedative laxative tablet being given every 2 hours on the odd hour during the day (9 tablets daily). By this treatment 14 liters of *N*/10 hydrochloric acid were neutralized per day in an attempt to neutralize the corrosive effects of acid for a period of 4½ months. Treatment may be considered adequate if the patient with ulcer, who is first seen on an ulcer diet and in distress, is able to have an unlimited diet, without symptoms, in 24 hours. Of the 3,877 patients, the ulcers appeared to heal in 83.4%. There remained, however, 16.6% who could not tolerate an unrestricted diet even though taking full therapy, as outlined above. In this group neutralization had to be increased to 19.5 liters of *N*/10 hydrochloric acid. Results showed that in 7.62% of the patients the ulcers could not be healed, and the patients could not be made symptom-free no matter what amount of alkali or adsorbent was used.

The author contacted 1,036 patients who were treated up to July 1, 1955. All these patients had enjoyed 34 or more months of relief from the hyperacid syndrome while taking no medication and eating an unrestricted diet. In an average of 34 months symptoms had recurred in 446 patients, while in 590 patients symptoms had not recurred in 4 years and 10 months. The use of follow-up roentgenograms as a criterion of healed ulcer is probably inadequate. Unrestricted diet was found to be useful in determining adequate treatment, in determining the time of recurrence of ulcer, and in defining medical failures.

Prognosis of Patients Surviving First Clinically Diagnosed Myocardial Infarction. J. L. Juergens, J. E. Edwards, R. W. P. Achor, and H. B. Burchell. A. M. A. Arch. Int. Med. **105**:444-450 (March) 1960 [Chicago].

The authors report on 212 men and 67 women, all of whom were residents of Rochester, Minn., and who were selected as having had their first acute myocardial infarction, the diagnosis of which was made at the Mayo Clinic between 1935 and 1951. The average age at the onset of acute infarction was 62 years for all the patients—60 years for men and 67½ years for women. Forty-four of the 279 patients died within one month from the effects of the acute infarction. Follow-up information was obtained concerning 224 (95%) of the 235 survivors. Among the traced patients, 154 (68.8%) survived for 3 years; 55.4% survived for 5 years, and 29.2% for 10 years. Five-year survival rates were more favorable in the younger age groups and in the men. Five-year survival rates in relation to the presence or absence of angina pectoris, hypertension, and congestive heart failure before the infarction were calculated, and these factors, when present, were found to have an unfavorable influence on the prognosis. Whether the occupation was physically strenuous seemed to have little effect on survival. The degree to which the patient was able to resume preinfarction activity appeared to be the best prognostic indicator.

Autopsy was performed on 82 patients, or on 65% of those in whom death was known to have occurred. On pathological examination, the hearts of 3 of these patients proved not to have healed infarcts. Among the other 79 patients in whom healed infarcts were found, anterior location of the infarct was observed in 41 (52%), i. e., the most common location; posterior infarction, which was observed in 33 patients (42%), was somewhat less frequent, while infarctions of the lateral wall in 4 patients (5%) and of the ventricular septum in only

1 (1%) were uncommon. Subendocardial infarction was observed in 54% of the hearts, and transmural infarction in 46%. The cause of death was primarily cardiac in 65 (82%) of the 79 patients on whom autopsy was performed. These 65 patients were divided into 3 categories; death was due to myocardial failure in 17 and to recurrent acute myocardial infarction in 27; in 21 sudden death occurred from other cardiac cause than cardiac failure or myocardial infarction. Recurrent acute myocardial infarction thus was the most frequent single cause of death in this series, but the other 2 categories had significant numbers also. The greater incidence of cardiac death in this study suggests that the clinically recognized cases of acute myocardial infarction may be, as a rule, the more severe cases of coronary artery disease.

Urticaria Pigmentosa with Visceral and Skeletal Lesions. C. W. H. Havard and R. B. Scott. Quart. J. Med. 28:459-470 (Oct.) 1959 [London].

A 67-year-old woman was admitted to St. Bartholomew's Hospital, London, in December, 1956, with a complaint of abdominal pain, lassitude, and swelling of the ankles. Twelve years previously a claret-colored eruption had appeared on the skin of the chest, and had spread within 10 months to cover the body. Biopsy at that time had established the diagnosis of urticaria pigmentosa. For 10 years she had suffered from attacks of epigastric pain and flatulence, sometimes accompanied by diarrhea. On admission to another hospital 3 years previously, splenic and hepatic enlargement had been noted. In the past 6 months there had been increasing lethargy, weakness, abdominal discomfort, and swelling of the ankles. The authors describe numerous investigations carried out on this patient in whom urticaria pigmentosa was associated with lesions in the bones, due to infiltration with mast cells, and with enlargement of the liver and spleen. Nineteen other reported examples of this syndrome are reviewed.

Urticaria pigmentosa, like other diseases originally regarded as merely dermatological, is discovered to be a systemic disease. Enlargement of lymph nodes, liver, and spleen, defects of coagulation, and skeletal changes have all been recorded in association with the characteristic eruption of urticaria pigmentosa. The basic anatomic change is a multiplication of mast cells in certain tissues of the body, notably the skin, bone marrow, lymph nodes, spleen, and liver.

The morbid changes produced are peculiar to cells of mesenchymal ancestry, and the disorders fall into 5 groups. First, there are the systematized diseases of reticular tissue which are neoplastic, and to which the term "reticulosarcoma" may be applied. The 2nd group includes the leukemias, Hodgkin's disease, and the related complaints which may be called the reticuloses, that frequently misapplied label being used to denote "a group of diseases of reticulum in which proliferation is followed by differentiation into one or several of the possible cell progeny." A 3rd group, to which the name "reticulosis" is equally applicable, comprises those lipoidoses which are apparently accompanied by a disorder of intracellular lipid metabolism—Gaucher's and Niemann-Pick's diseases. The 4th class consists of what was once called the "storage-reticuloses," in which histiocytic proliferation is a response to some extracellular perversion of metabolism; the hypercholesterolemic xanthomatoses provide familiar examples. Finally, systematized reactions of reticular tissue are evoked by some infections, and perhaps the most striking instance is kala-azar.

The systematized mast-cell disease, urticaria pigmentosa, must fall into one of these 5 categories. The authors feel that it should be included in the 2nd class, and perhaps the name "mast-cell reticulosis," while solving no problems of etiology or pathogenesis, best indicates the nosological position.

Primary Aldosteronism: Reports of 2 Cases and Review of the Literature. R. T. Manning, M. H. Delp, C. F. Kittle, and others. J. Kansas M. Soc. 61:165-171 & 188 (March) 1960 [Topeka].

The syndrome resulting from excessive reduction of aldosterone by the adrenal was first described by Conn in 1955, and about 32 cases have been reported. The authors report 2 additional cases; both patients were women, one, aged 43 years, and the other, 51. In the 2nd patient the spirolactone, SC-9420 (Aldactone), was given during a balance study when primary aldosteronism was suspected. There was evidence that the drug blocked the effect of aldosterone on the renal tubules. Adrenal adenomas were found and removed in both women, and the results of the operations were excellent.

The authors tabulate data on the 32 cases collected from the literature and on the 2 presented here. Twenty-eight of the 34 patients had adrenal adenomas, of which 7 were on the right and 19 were on the left side; 2 were not reported as to location. Four patients had adrenal hyperplasia alone, and 2 had adrenal carcinomas. All the patients had hypertension, and most showed electrocardiographic changes consistent with hypopotassemia. Intravenous pyelograms did not contribute to the diagnosis, whereas retroperitoneal air study frequently demonstrated a tumor. All showed at least one serum specimen that was abnormally low in potassium, and many showed increased sodium and increased carbon dioxide content. Hyposthenuria was a consistent finding, as was impaired urinary acidification with excretion of an alkaline urine. Elevation in aldosterone excretion was noted, with the majority showing 17-hydroxy and 17-ketosteroid excretion in the normal range. Left-sided tumors were almost 3 times as frequent as those on the right. No extra-adrenal lesions have been reported. With this in mind, it would seem best to use the posterior approach because of its technical facility as compared with abdominal exploration.

SURGERY

Treatment of Anorectal Malignant Melanoma. G. T. Pack and F. G. Martins. Dis. Colon & Rectum 3:15-24 (Jan.-Feb.) 1960 [Philadelphia].

The authors report on 6 women and 1 man, between the ages of 50 and 68 years, with anorectal malignant melanoma, all of whom had already had a conservative local operation. Since the anorectal melanoma tends to recur locally and to metastasize to regional lymph nodes with great frequency, the application of radical surgical principles is imperative. The operation performed by the authors at the Memorial Center for Cancer and Allied Diseases in New York consisted of a one-stage abdominoperineal rectal resection, pelvic lymph node dissection, and bilateral dissection of inguinal and femoral nodes in continuity with the anus, by removing a wide strip of skin, subcutaneous tissues, and fascia intervening between the groins and the perineum. The interval between biopsy and this radical operation varied from 7 to 60 days. In 3 of the female patients a total hysterectomy with bilateral salpingo-oophorectomy was performed in order to afford a more thorough pelvic lymph node dissection.

Of the 7 patients, 4 died within 4 to 14 months after the operation. Death resulted from metastasis to the lungs, spine, brain, retroperitoneum, and liver respectively. One patient died of atelectasis and ileus within 48 hours postoperatively. Two patients are alive, 30 and 32 months after the operation; one has melanoma, but the other is free of the disease. Nineteen patients with malignant melanoma of the anorectum were reported on by one of the authors in a previous paper in 1952; all these patients died. The prognosis for anorectal melanoma is bad because of 4 factors: inadequacy of early treatment; delay in diagnosis; rapidity of dissemination of the cancer; and high degree of malignancy.

Acute Osteomyelitis Treated with Large Doses of Antibiotics. P. E. Johansen and V. Lund. Ugesk. laeger 122:78-84 (Jan. 21) 1960 (In Danish) [Copenhagen].

The increasing frequency with which yellow staphylococci, producing penicillinase, are the etiological factor in acute osteomyelitis has necessitated treatment with massive doses of penicillin supplemented by other forms of antibiotic therapy. Even when the antibiotic treatment seems to be successful, grave complications can be seen, and bone resorption with spontaneous fractures is especially to be feared. In the second half of 1958, 3 patients with acute osteomyelitis were treated with antibiotics in Marselis Hospital, in Denmark. The 1st patient had had a grave acute osteomyelitis; there had probably been recurrence, and the process is perhaps not yet at rest. Treatment was exclusively with antibiotics in the hope that, by omitting surgical treatment, the risk of secondary infection and sequestration of the femur might be avoided. In the 2nd patient moderately grave osteomyelitis subsided on treatment. In the 3rd patient early and intensive treatment of acute osteomyelitis was given. Long-continued treatment with massive doses of penicillin was applied, combined with other suitable antibiotics chosen, as far as possible, by determination of resistance. The sedimentation reaction was the guide for the duration of the treatment.

Pheochromocytoma. L. Arin, Y. Isgren, and C. G. Aman. Nord. med. 63:138-139 (Jan. 28) 1960 (In Swedish) [Stockholm].

In a woman, aged 48 years, who had been well until 1950, intermittent attacks of hypertensive crises set in, which became increasingly frequent and severe, with high urinary output of pressor substances. There were hypochromic anemia, normal sedimentation reaction, intermittent albuminuria and slight bacilluria. Transperitoneal resection of a typical pheochromocytoma, the size of a small orange, from the left adrenal was done. The tumor was not malignant. The postoperative course was uneventful, with prompt return to normal output of urinary catechols. Moderate hypertension persists, but the renal function is intact.

Primary Carcinoma of the Lung: A Follow-Up Study Including Pulmonary Function Studies of Long-Term Survivors. J. C. Jones, J. L. Robinson, B. W. Meyer, and H. L. Motley. J. Thoracic & Cardiovas. Surg. 39:144-158 (Feb.) 1960 [St. Louis].

The purpose of this paper is twofold: (1) to present data on the fate of patients operated on for primary carcinoma of the lung and (2) to call attention to the cardiopulmonary illness faced by those who were successfully treated by pneumonectomy. Thoracotomy was performed because of primary carcinoma of the lung on 513 private patients between July, 1942, and January, 1959. The group included 68 (13.3%) women. Exploration only was carried out in 229 cases, with a mortality of 0.4%. Of the remaining 284 patients, lobectomy was performed on 87, with 1 death (1.1%), and pneumonectomy on 197 with 13 deaths (6.6%), giving an over-all resection mortality of a little under 5%. Three of the 13 deaths after pneumonectomy were of patients over 70 years of age.

An increased use of routine chest x-ray examinations during the last half of the study has resulted in bringing in more people with peripheral asymptomatic lesions, and in an increase in adenocarcinoma in the resected specimen from 12.8 to 18.1% Probably for the same reason, there has been an increase in the proportion of women from 12.2 to 13.9%. Twenty per cent of the 150 patients who underwent pneumonectomy survived for 3 years or more. Of 52 patients on whom lobectomy was performed, 51.9% survived for 3 years or more.

Especially interesting were 63 patients who underwent pneumonectomy 10 or more years ago. Of the 33 who survived one year, 15 died later of carcinoma, but 7 died of causes other than carcinoma, and the majority of these deaths was attributed to cardiac failure. This fact prompted the authors to study the cardiopulmonary function of the 11 survivors. Complete pulmonary function studies could be carried out on 9 of the 11 patients. Although all but one of these were living satisfactory lives, and either working or reasonably active, they all had some cardiopulmonary disability. The function studies indicated that, except for one case, pulmonary emphysema was not a significant problem; nor was distention of the remaining lung. The abnormalities which appeared to be responsible for disability were pulmonary fibrosis, bronchospasm, and increased resistance of the pulmonary vascular bed. Although not proved by cardiac catheterization, pulmonary hypertension was inferred to exist. Right heart disease appeared to be the greatest problem faced by these long-term survivors of pneumonectomy. Additional studies directed toward determining causative factors are needed.

The Natural Course of Arteriosclerosis of the Lower Extremities. A. M. Boyd. Angiology 11:10-14 (Feb., part 1) 1960 [Baltimore].

The critical evaluation of any type of treatment should be made against the background of the natural course of the disease, particularly in a generalized progressive disease like arteriosclerosis; otherwise, reconstructive operations upon segmental occlusions are difficult to evaluate. The author investigated the natural course of intermittent claudication in patients suffering from it but having no gangrene or pregangrenous changes. The patients attended a special follow-up clinic. Of 1,440 patients, 144 (10%) were women. The average age when first seen was 57.2 years, and 70% of the patients were between 55 and 74 years old.

It was found that the chance of survival for 5 years for all patients is 73.5%, but this change is almost halved for 10 years (38.8%), and almost halved again for 15 years (22.0%). In 105 patients gangrene occurred, requiring mid-thigh amputation. This figure includes 8 bilateral amputations. Nonfatal coronary or cerebral occlusions occurred in 301 patients. The chance of one of these incidents in the first 5 years is highest in the 2 age groups, 45 to 54 and 55 to 64 (22.0% and 21.9%, respectively), and is roughly doubled in the first 10 years. A further thrombosis in either leg occurred in 298 patients, an important fact to remember before undertaking any radical operation on a solitary segmental thrombosis. The initial success rate of thromboendarterectomy is 60 to 70% and of bypass grafting somewhat higher. The late success rate seems to be maintained after thromboendarterectomy but tends to fall after bypass grafting.

From his investigation into the natural course of the disease, the author makes a rough estimate of the number of patients in whom surgery on the obstructed segment might be reasonably considered but not technically possible. Twenty-five of 100 patients seen within one year of the onset of intermittent claudication will be 65 or more years old, which leaves 75 patients. Coronary or cerebral episodes will have been suffered by 8%. About 25% of the remaining 69 patients will have a diastolic pressure of 100 mm. Hg or more. Of the remaining 52 patients, 13 will have diffuse arteriosclerotic changes but no segmental thrombosis. About 18 will have thrombosis of the popliteal artery and, therefore, be unsuitable for reconstructive procedures, leaving 18 patients with a femoral and 3 with aorticoiliac occlusions. At least half of those with femoral occlusions are found to have arteriosclerosis of the vessels in the distal half of the leg of sufficient severity to contraindicate bypass grafting. At least 1 of the 9 will have more diseased distal vessels than the arteriogram indicated. Of the 3 high blocks, 2 will probably be operable. From this rough estimate it would seem that only about 10 of 100 cases would be suitable for reconstructive surgery.

The patient may not want to have a major operation to make him able to walk farther, because he normally does very little walking; many patients are content with the increase in their walking distance gained by walking more slowly. There is a great deal to be said for conservative management of arteriosclerosis and in being content to allow patients to grow old gracefully.

Experiences with Sterilization Tests of Catgut. M. Fischer. Chirurg. 31:52-58 (Feb.) 1960 (In German) [Berlin].

On Sept. 18, 1951, the Minister of Public Health issued a decree, according to which the production of catgut was to be controlled by the government in East Germany. Up to June, 1959, 6,455 packages containing 12,910 meters of catgut were subjected to sterilization tests by government laboratories. Clostridium tetani was not found in any of these packages, and not a single case of postoperative tetanus due to infected catgut was observed by the author in the course of a 10-year period. No anaerobes pathogenic to animals, and, therefore, no clostridia either, were found in a large series of tests performed on 30 catgut coils (617.7 meters), which had been produced by catgut manufacturers in the German Democratic Republic. These tests revealed a contamination rate of 50 tubes among 41,182 liver bouillon tubes in whose broth a small thread of catgut had been placed, i. e., one spore (aerobic or anaerobic) was detected in 12.4 meters of catgut. By assuming that one spore requires 10 μ of catgut thread, a contamination rate of 0.000008% was calculated; besides this very small rate, the spores were not pathogenic. Two healthy sheep then were killed, and the contents of the small intestines (from which catgut is made) were subjected to bacteriological tests. Only a single Clostridium organism was found among 2,000 anaerobes, and consequently the worst risk of infection with Cl. tetani, expressed in percentage, would be 0.0000000046.

These data indicate that the fear of surgeons that the employment of catgut for sutures might involve the risk of surgical tetanus is apparently unwarranted, since such a risk is improbably small. While some years ago complaints by surgeons concerning suspected nonsterility and deficient firmness and absorption of catgut were numerous, these complaints have diminished, but will never cease completely. For common suppuration after suture of wounds catgut cannot be made immediately responsible, because the so-called classic causative agents of pus are destroyed in any case by today's sterilization methods. If catgut, like any other suture material, absorbs pus germs in the course of the surgical intervention, the catgut acts only as a mediator, as does any other surgical device. Suppuration of sutures results from several hereditary and environmental factors, which are peculiar to the patient and which depend on his actual disposition ("stress-situation"). Hospitalism and carrier state (patient and hospital staff) also play an important part.

Conn's Syndrome: "Primary" Hyperaldosteronism Due to Adenoma of the Adrenal Cortex. F. Siguier, E. E. Baulieu, C. Betourne, and others. Semaine hôp. Paris 36:603-614 (Feb. 28) 1960 (In French) [Paris].

The authors report a 45-year-old woman who had arterial hypertension of 14 years' duration. Clinically the condition was dominated by extreme general weakness, emaciation, spasms, polydipsia, and paretic episodes characterized by regression and relapses. The renal manifestations, consisting of potassium depletion, polyuria, albuminuria, significant isosthenuria, and absence of edema, completed the syndrome originally described by Conn. There was a persistent hypopotassemia and an increased pH. Aldosterone excretion in the urine was found to be significantly elevated above normal values, whereas the values of 17-ketosteroids and 17-hydroxysteroids were normal. Based on these findings, an adrenal exploration was decided upon, although the examination by means of retroperitoneal insufflation did not clearly show a pathological enlargement in the size of the adrenal cortex. The operation revealed that the right adrenal was highly hypoplastic; a walnut-sized adenoma was found to involve completely the left adrenal gland, which was resected.

The postoperative course was characterized by a dramatic improvement in the patient's condition, with the disappearance of all symptoms and signs within 8 days after the operation. The patient was not given any particular preoperative medication, but she received during 4 days after the operation a total of 250 mg. of cortisone. The follow-up examination of the patient 18 months after the operation showed that she was in perfect health. The studies on the abnormal sodium and potassium metabolism in this patient showed that the variations in aldosteronuria did not explain all the changes in the sodium values; there was no parallelism between aldosteronism and sodium retention. The potassium values, however, progressed with remarkable consistency parallel with the sodium values; if the changes in the sodium values were due to aldosterone alone, then the modifications would be systematically opposed.

Acute Fulminating Ulcerative Colitis with Colonic Distention. G. W. Peskin and A. V. O. Davis. Surg. Gynec. & Obst. 110:269-276 (March) 1960 [Chicago].

The authors report on 6 women and 3 men, between the ages of 18 and 40 years, with acute fulminating ulcerative colitis with abdominal distention, who were operated on at the Hospital of the University of Pennsylvania in Philadelphia. Seven of the patients were white, and 2 were Negroes. With the exception of 1 patient who had a history of ulcerative colitis for 7 years, and 2 others whose disease had begun 5 years before admission, the patients were believed to have had the disease for less than 1 year. The acute phase had been present for one week or less in 6 of the 9 patients. In 7 patients the colon had already perforated at the time of the surgical intervention. Each of the patients first received a trial of intensive medical therapy; 6 of the 9 patients were given steroid therapy before the surgical intervention, but this therapy did not alter the pathological process.

The operative treatment in 6 patients consisted of an immediate subtotal or total colectomy and the establishment of an ileostomy. In one patient the procedure was limited to a transverse colostomy, primarily because the patient was in her 6th month of pregnancy, and it was considered unwise to carry out a colectomy for fear of interruption of the pregnancy and excessive bleedings from the engorged pelvic veins. One additional patient was treated by ileostomy alone, and the postoperative course was so poor that abdominal colectomy was required within one month. In the last patient decompression was accomplished by colostomy, and an ileostomy was established; this patient required a colectomy at a later date because of abscess formation within the peritoneal cavity. In all these patients progress was good as far as the underlying disease process was concerned, with the exception of the patient who had ileostomy alone. One patient with colectomy and ileostomy died of massive gastrointestinal bleeding from a duodenal ulcer, and another died after an abdominoperineal resection of the rectal stump 2½ years after the initial subtotal colectomy. The one patient treated by transverse colostomy has had several exacerbations of the disease, and each time refused surgical intervention. There was no further evidence of an acute fulminating process.

A review of the literature showed that controversy still exists concerning the therapy of acute fulminating ulcerative colitis. Many recent reports have substantiated the good results which can be achieved with the more radical approach of combined ileostomy and colectomy. The over-all mortality for patients with acute fulminating ulcerative colitis treated by the medical method is 57%; ileostomy alone, 50%; and ileostomy and colectomy, 15.9%. These figures, although selective to a degree, should serve to stimulate a more radical approach to these patients at an early period in their disease process.

Transthoracic Vagotomy for Stomal Ulceration. C. Wells and R. Silberman. Lancet 1:406-407 (Feb. 20) 1960 [London].

The authors report on 17 men and 6 women, aged from 28 to 73 years, who underwent transthoracic vagotomy at the Royal Infirmary, Liverpool, for stomal ulcers, which developed after gastroenterostomy in 4 patients, and after gastric resection in 19. Transthoracic vagotomy relieved all 4 patients who had had previous gastroenterostomy of their ulcer symptoms, and they were all well at the time of follow-up. In 13 of the 19 patients with previous gastric resection all symptoms were removed by the thoracic vagotomy, and 11 of these patients were well at the time of follow-up. The other 2 had died of unrelated causes.

Transthoracic vagotomy is simple and safe. The reported data show that it is probably the best means of treating stomal ulcers occurring after otherwise uncomplicated gastrectomy or after gastroenterostomy, provided that the stoma is well placed and functioning satisfactorily. The diagnostic proof of stomal ulcers is not always easy. Estimation of night secretion, which was not routinely available at the time these patients were studied, may prove invaluable. Persisting acidity is a reasonable indication for vagotomy. On a priori grounds, vagotomy is necessary in operations of the Billroth 1 type for duodenal ulcer. If acidity persists after abdominal vagotomy, thoracic vagotomy should be undertaken as an adjuvant. In patients who have undergone bizarre or multiple operations on the stomach and duodenum, the surgeon must weigh the dangers and complications of a further abdominal operation against the advantages of actually seeing the lesion. In the presence of pain suggestive of ulcer, and of continued night secretion of acid, thoracic vagotomy is safe and worthwhile. In some late and complicated cases, disappointments are inevitable whatever is done.

Pneumonectomy for Tuberculosis: An Evaluation of 124 Cases. J. E. Hiltz, V. D. Schaffner, and G. A. Kloss. Canad. M. A. J. 82:457-463 (Feb. 27) 1960 [Toronto].

The authors analyzed the results of pneumonectomies performed on 124 patients at the Nova Scotia Sanatorium, in Kentville, between 1945 and 1959. Male and female patients were evenly divided. Their ages ranged from 11 to 56 years, with a preponderance in the decades between 20 and 50 years. Operations were carried out on the right lung in 51 patients and on the left in 73. Far-advanced disease within the lung on the operative side was present in 95 patients; in 29 the disease was moderately advanced. In 47 patients the contralateral lung was free of disease, in 54 patients it showed a minimal degree of tuberculosis, and in 23 tuberculosis was moderately advanced. In all patients the contralateral tuberculous lesion was considered to be well controlled, and in most patients the homolateral disease was well stabilized before surgery was undertaken.

Of the 124 patients, 57 developed a total of 135 complications postoperatively. Complications included the development of a bronchopleural fistula either early (within 4 weeks after operation) or late; a stubborn, persisting pleural space; an empyema; moderate or severe wound infection; and residual ulcer of the bronchial stump seen bronchoscopically. In some instances death occurred too early for complications to become evident. Most of the complications occurred in patients between 50 and 59 years of age, and particularly in men over 20 years of age. Complications were 2 or 3 times as frequent in patients in whom cavitation was present preoperatively as in those in whom no cavitation was then present. The larger the cavity, the greater was the tendency for the development of complications. It was found that operations performed on the right lung carried a greater hazard than those performed on the left. Of 51 operations on the right lung, 30 resulted in complications, while of 73 operations performed on the left, only 27 were followed by complications. The presence of previously existing tuberculous tracheobronchitis, as seen bronchoscopically, did not greatly influence the development of complications, which may be due to the fact that antimicrobial therapy was used extensively to bring such lesions under control before surgery was carried out. Of 108 patients who were followed up 2 years after the operation, 51 were greatly improved, and 24 were moderately improved. A test of the sputum of these 75 patients gave a negative result. Of 84 patients who were followed up 5 years or more after the operation, 46 were greatly improved, and 6 were moderately improved. The sputum test of these patients also showed a negative result. Only 6 of 35 patients who were followed up after 10 years were still alive. Twenty-one had died of tuberculosis, and 8 of nontuberculous causes.

Post-Traumatic Intussusception in Adults. J. A. Dixon. Am. Surgeon 26:99-101 (Feb.) 1960 [Baltimore]

Intussusception occurs in adults, as a rule, only in association with polyp, carcinoma, or diverticulum; idiopathic or primary intussusception is rare. The author presents the histories of 4 men in whom intussusception was observed. The 1st patient had received a gunshot wound in the abdomen. At laparotomy 2 penetrating wounds of the cecum were found. On exploration of the small intestine an antegrade intussusception of the ileum was found, which was approximately 16 cm. in length. Upon reduction of the intussuception there was no evidence of an intraluminal mass. The 2nd patient, a 76-year-old man, had been struck by a truck, receiving a severe abdominal contusion, a fracture of the left ulna, and a partial avulsion of the scalp. Shock and abdominal rigidity were evident. At laparotomy the patient was found to have a transection of the transverse colon. Exploration of the small intestine revealed an antegrade intussusception, 22 cm. in length and easily reduced. No tumor or trauma was noted in the region of the intussusception. The colon ends were exteriorized. The postoperative course was uneventful. These 2 cases presented no diagnostic problem. Surgical treatment was indicated, and the intussusception was an incidental finding. There was no evidence of recurrence after reduction.

Cases 3 and 4, on the other hand, presented difficult diagnostic aspects. The 3rd patient had undergone transorbital lobotomy for paranoid schizophrenia. Six hours after the lobotomy he complained of severe crampy abdominal pain, nausea, and vomiting, and became moderately distended. The picture for the next 5 days was one of intermittent partial intestinal obstruction. There was intermittent improvement, but on the 16th postoperative day severe intestinal obstruction was evident, and a tender mass was palpable on rectal examination. A laparotomy was performed, and an antegrade intussusception of the ileum was found, approximately 14 cm. in length, extremely firm, fibrotic, and irreducible. A resection of the ileum with anastomosis was performed. The intussusception showed no tumor or diverticulum. The 4th patient was involved in a trench cave-in. He sustained injuries to several lumbar vertebrae and severe contusions of the abdomen. Examination of the small intestine during laparotomy disclosed 3 antegrade intussusceptions in the lower jejunum. Each of these was approximately 10 cm. in length and easily reduced. However, the postoperative course was marked by evidence of intermittent intestinal obstruction. A laparotomy was performed 24 days after the original injury, and an antegrade jejunal intussusception was found, which was 13 cm. in length and not reducible. The intussusception was resected, and an end-to-end anastomosis performed. Examination of the specimen showed no tumor or diverticulum. On the basis of a review of the literature, this 4th case, in which intussusception recurred postoperatively and required resection, seems unique.

Surgical Indications in Cholelithiasis: Prophylactic Cholecystectomy Elucidated on the Basis of Long-Term Follow-up on 526 Nonoperated Cases. J. Lund. Ann. Surg. 151:153-162 (Feb.) 1960 [Philadelphia].

In patients with gallstones the presence of biliary colic and of complications is generally accepted as an indication for cholecystectomy or other interventions on the biliary tract. Opinions differ with regard to the indications for prophylactic cholecystectomy in the presence of stones in order to prevent future symptoms and complications. The author presents observations on 526 patients with gallstones who were not operated on and who were followed up for from 5 to 20 years after the discovery of the stones. Only patients with roentgenologic signs of gallstones were included. In 100 patients the gallstones were accidentally discovered during roentgenologic examination of the abdomen. The complete series includes all patients with cholelithiasis admitted to the Copenhagen County Hospital, Gentofte, Denmark, from 1936 to 1950, who were not subjected to cholecystectomy. Since 1950 more than 90% of cholelithiasis patients have been subjected to cholecystectomy, but this was not the case before 1950. The 526 patients included 388 women and 138 men. Twenty-five per cent of the patients died during the period of follow-up. The data on 50 patients were inadequate, and these were disregarded in some of the analyses.

It was found that, irrespective of the severity of the clinical aspects at the time of the diagnosis of gallstones, severe symptoms or complications developed subsequently in at least one-third to one-half of the patients, and complications in the form of acute cholecystitis or common duct stones occurred in at least 25%. The prognosis for patients with asymptomatic stones, according to previously published opinions and to the findings in this series is about the same as for those who have symptoms.

The mortality in patients with cholelithiasis was 2.7%, but subsequent operation has prevented a number of deaths. There was a marked increase in mortality with advancing age. Beyond the age of 60 mortality was 7.2%. Cancer of the gallbladder occurred in 3 cases. The risk of the development of cancer of the gallbladder in the presence of cholelithiasis was found to be no higher than the surgical mortality of elective cholecystectomy. Thus, although the risk of cancer as such does not require prophylactic cholecystectomy, it is, nevertheless, an additional factor militating for surgical treatment.

The author concludes that prophylactic removal of the gallbladder is indicated in all patients with gallstones who are reasonably good surgical risks. This will prevent much future morbidity. With the present low mortality of elective cholecystectomy, primary operation is likely to carry a lower mortality than nonoperative treatment.

Assessment of the Results of Surgical Treatment in Portal Hypertension. A. I. Macpherson. Gastroenterology 38:142-154 (Feb.) 1960 [Baltimore].

The author treated 118 patients who had portal hypertension at the Edinburgh Royal Infirmary. Of these, 22 had extrahepatic and 96 intrahepatic obstruction. A satisfactory answer to the question as to whether the surgical treatment of patients with portal hypertension associated with chronic hepatic disease is beneficial cannot yet be given. The results of medical treatment in a similar series of patients at the Mayo Clinic were compared with those in this series. The available data indicate that only in the first postoperative year has surgical treatment shown beneficial results. It always has an immediately adverse effect on the functioning of the cirrhotic liver, but it seems that the degree and duration of this effect depend chiefly on the condition of the liver at the time of operation. Moreover, if the patient has survived the immediate postoperative period, the liver recovers and appears to regain a functional capacity, even when the operation has entailed the diversion of all the portal blood from the cirrhotic liver cells.

Whether correction of thrombopenia or granulopenia is sufficiently important to justify splenectomy is still controversial, but it appears that when there is persistent thrombopenia, the improvement of the hemostasis alone, which is obtained by including splenectomy as part of the definitive operation for portal hypertension, outweighs the possible disadvantages. Hematemesis is such a dramatic occurrence that comparison of the number of instances of it, both before and after operation, suggests itself as the most decisive measurement of the value of surgical treatment. However, in many of the medically treated patients hematemesis is a terminal event, and the unpredictability of bleeding in patients with portal hypertension makes deductions drawn from retrospective comparison of its incidence before and after operation of doubtful significance. Even the effect of splenectomy on the blood dyscrasia is controversial, since the presumptive benefit arising from it cannot readily be measured. The author believes that the problem of when, or even whether, to operate on patients with gastroesophageal bleeding and severe impairment of hepatic function can be solved only by experience and experiment. Each case should be considered not only as that of a patient to be relieved, but also as a source of information to be thought about objectively, recorded, and dispassionately reviewed.

GYNECOLOGY & OBSTETRICS

Fluorescent Antibody Tests for Detection of the Gonococcus in Women. W. E. Deacon, W. L. Peacock Jr., A. Harris, and others. Pub. Health Rep. 75:125-129 (Feb.) 1960 [Washington, D. C.]

The successful application of the fluorescent antibody (FA) method for the identification of Neisseria gonorrhoeae in men prompted an investigation of the use of this method for the detection of gonococci in women, the more so since the culture methods available are slow, cumbersome, and costly. The aim of this study was the development of a rapid FA procedure for N. gonorrhoeae detection, capable of obtaining equal or superior results to those reported for the culture method. Women, constituting the study group, were named contacts of men with gonorrhea seen at the clinic of the division of veneral disease control, Fulton County Health Department, Atlanta, Ga.

The authors describe a direct FA method, a delayed FA method, and a culture method for the detection of the gonococcus in women, specimens being obtained from the vagina, cervix, and urethra. The results obtained with these methods in 50 women contacts are compared in a table. Direct FA identification of the gonococcus in women may be accomplished in approximately one hour. However, N. gonorrhoeae detection by this method is dependent upon the quantity of pathogens at the site at the particular time of examination. This factor is minimal when the delayed FA procedure is used. A combination of the direct and delayed FA methods was clearly demonstrated as superior to the conventional culture method. The delayed FA method gave a slightly higher yield of positive results in less time than the conventional culture method. The delayed FA method was superior to the direct method alone. The value of vaginal examinations, in addition to the customary urethral and cervical tests, is indicated.

Intrinsic Fetal Risk in Breech Delivery. M. G. Potter Jr., C. E. Heaton, and G. W. Douglas. Obst. & Gynec. 15:158-162 (Feb.) 1960 [New York].

There were 1,256 breech presentations (4.2%) among the 29,969 deliveries which occurred on the obstetric service of Bellevue Hospital in New York from 1945 to 1956. The authors reviewed 1,142 of the 1,256 cases of breech presentations and analyzed the intrinsic risk involved in this type of delivery. Prenatal care was given to 57.1% of the patients, i. e., to all primiparas in whom a breech presentation was detected, during or shortly before the onset of labor, by stereoscopic x-ray pelvimetry. The method of delivery included pudendal block anesthesia, supplemented by nitrous oxide or gas-oxygen-ether. Cesarean section was performed on 110 patients; in 62 of these, breech presentation was a determining factor in choosing the type of intervention. There were 3 fetal deaths (4.8%) in this group.

There were 141 nonviable infants (weight at birth under 1,000 Gm. [2 lb. 3 oz.]) and 13 fetal deaths attributable to breech delivery. The fetal mortality was 5.1% among primiparas and 1.5% among multiparas. The only maternal death in the whole series occurred in a primipara with rheumatic heart disease. Autopsies on 12 of the 13 infants whose deaths were attributable to breech presentation showed a uniform picture of intracranial injury with hemorrhage. Yet only 3 infants had been delivered by extraction. The authors recommend a careful search for patients showing slight to moderate degree of disproportion and a more liberal use of cesarean section as a means of lowering fetal mortality in breech presentation.

Acute Renal Failure in Obstetric Patients: Treatment by Hemodialysis. S. Anthone, R. Anthone, and J. E. Doyle. Obst. & Gynec. 15:146-157 (Feb.) 1960 [New York].

The various etiological factors and the main aspects of management in acute renal failure during pregnancy or at delivery are reviewed. A total of 29 patients with acute renal failure were treated at the Buffalo General Hospital from 1954 to 1958. Eleven patients (38%) had renal failure as a consequence of complications of pregnancy. The determining factor of the disease was transfusion reaction in 2 patients, afibrinogenemia and hemorrhage shock in 5, obstruction of a solitary kidney in 1, and eclampsia in 2. The patients were dialyzed from 1 to 3 times during the renal failure, and all of them eventually recovered their renal function.

Hemodialysis should be considered as an aid to medical management of patients in acute renal failure and should be applied whenever conservative measures no longer control the toxic effects of the renal shutdown. If acute renal failures are properly treated and dialyzed rather early than late in their toxic course, a high percentage of good results will be the rule in a condition that once was considered to have a high mortality rate.

The Pregnanediol Excretion in Suspected Placental Insufficiency. C. S. Russel, C. J. Dewhurst, and D. H. Blakey. J. Obst. & Gynaec. Brit. Emp. 67:1-10 (Feb.) 1960 [London].

The urinary pregnanediol excretion was studied in a group of 58 patients in whom placental insufficiency had been diagnosed or was suspected to be present. Most of the patients either suffered from hypertension or preeclampsia or gave a history of a previous stillbirth believed to be due to placental insufficiency; a few patients had no such associated abnormalities. The clinical diagnosis of placental insufficiency was based on the finding of a small child who did not grow normally; normal size and growth of a child are regarded as evidence of good placental function. In 16 cases (group 1) a confident diagnosis of placental insufficiency was made, and in 14 (group 2) there was no significant placental damage; in the remaining 28 cases (group 3) it could not be decided on clinical grounds alone whether there was placental insufficiency or not. Pregnanediol studies were carried out in all these cases. In group 1, in 14 cases low readings confirmed the diagnosis, and in 2 cases normal readings demonstrated good placental function which was subsequently confirmed. In group 2, normal readings were obtained in 13 cases, apparently confirming the diagnosis, and in the remaining case low readings suggested some placental damage. In one of the 13 cases an unexplained fetal death in utero occurred. In group 3, readings within the normal range, though below normal average, showed reasonable placental function in 10 cases; low readings showed placental insufficiency in 15 cases, while in 3 cases equivocal results were obtained.

Taking all 3 groups together, there were 30 cases with low readings. In all these, there was evidence of enough placental damage to affect the child.

Eleven babies were stillborn, and 2 died in the neonatal period; all the babies were below average in weight for the stage of pregnancy. The placentas were small and, in addition, showed evidence of infarction which was sometimes very severe. By contrast, in the 25 cases with normal values there was one unexplained death, and the weights of the babies (with this one exception) and of the placentas were normal.

The authors believe that, when placental insufficiency is a possibility either because of the previous obstetric history or because of the signs in the pregnancy under review, measurement of urinary pregnanediol is of great value. Sometimes this confirms the clinical diagnosis; at other times it compels a review of the clinical diagnosis, and occasionally provides startling evidence of the severity of the placental damage.

PEDIATRICS

Comparison of the Recurrence Rate of Rheumatic Carditis Among Children Receiving Penicillin by Mouth Prophylactically or on Indication: A Six-Year Study. W. Ngo Lim and M. G. Wilson. New England J. Med. 262:321-325 (Feb. 18) 1960 [Boston].

The American Heart Association has recommended that "all individuals with a well-established history of a previous attack of rheumatic fever or chorea, or who show definite evidence of rheumatic heart disease, should be placed on continuous prophylaxis throughout life or until new knowledge makes this recommendation invalid." This study was limited to children who had at least one observed attack of active carditis and were attending the cardiac rheumatic clinic of the New York Hospital. The recurrence rates of rheumatic carditis during the years 1952-1958 among 110 children receiving continuous penicillin prophylaxis orally (group 1) and 103 patients receiving penicillin therapeutically for only 10 days at the onset of any respiratory infection (group 2) were investigated. No attempt was made to evaluate the role of infection due to hemolytic streptococci in rheumatic fever or to investigate the incidence of streptococcic infection among rheumatic children receiving penicillin, but rather to determine whether continuous prophylaxis with orally given penicillin has any advantage over therapeutic administration of penicillin in the management of the rheumatic child.

The recurrence rate for continuous prophylaxis was 6.6 per 1,000 patient months for a total of 2,630 patient months. When calculated according to interval since last attack, it was 7.5 per 1,000 patient months for patients with recent attacks (less than 2 years), and 3.9 for those with an interval of more than 2 years since the last attack. The recurrence rate in the "indicated-therapy" group was 2.9 per 1,000 patient months for a total of 2,744 patient months. When calculated according to interval, the rate was 4.6 for recent attacks and 2.4 for those with longer intervals.

There was no significant difference in the recurrence rate of active carditis among patients receiving continuous oral prophylaxis and those on adequate penicillin therapy during a respiratory illness when the interval since the last attack was considered. For children under close medical supervision, continuous prophylaxis with orally given penicillin has no advantage over adequate penicillin therapy.

The Influence of Exogenous Iron on Formation of Hemoglobin in the Premature Infant. D. Hammond and A. Murphy. Pediatrics 25:362-374 (March) 1960 [Springfield, Ill.].

The present study was undertaken to evaluate certain variables which may influence early and late anemias in premature infants, and to determine the effect of parenterally administered iron in the neonatal period. Forty-eight infants born prematurely on the clinic service of the Herbert C. Moffitt Hospital of the University of California Medical Center were divided into 2 groups and were followed up for periods varying from 3 to 18 months. There were 22 infants in one group who served as untreated controls, and 26 in the other group who were given a total of 100 mg. of iron-dextran complex (Imferon) intramuscularly over a period of 2 to 4 days when the infants' weight had reached 1,500 Gm. (3 lb. 5 oz.) and weight gain was consistent. The mothers of the infants in the control group had an average age of 29 years; those of the treated group averaged 25 years. The estimated duration of gestation was 36 weeks for the control group, and 34 weeks for the treated group. The average birth weight of infants in the treated group was 1,980 Gm. (4 lb. 6 oz.), and of those in the control group 2,185 Gm. (4 lb. 13 oz.). Hematological studies were performed on all infants initially during the first 2 days of life, and were repeated between the 4th and 7th days weekly thereafter during the hospital stay, and monthly during visits to a clinic for healthy infants. The infants were given standard formulas of modified cow's milk, supplemented by vitamins A, D, and C in amounts sufficient to meet daily requirements.

Despite the fact that the initial hematological studies revealed slightly higher mean values for hemoglobin, hematocrit, and erythrocytes in the control group, a higher concentration of hemoglobin developed in the treated group before the 3rd month of life, and a significantly higher value was maintained from that time on throughout the period of the study. Although the infants in the control group averaged 205 Gm. (7¼ oz.) more in birth weight, their average weight gain during the period of observation was 48 Gm. (1½ oz.) less than in the treated group. It appears from these data that exogenous iron can be utilized by premature infants at an earlier age than generally assumed, at a time when the naturally acquired iron stores are not depleted. Early administration of iron appears to accelerate recovery from the early anemia of prematurity, and also can prevent the late anemia of prematurity. Dietary sources alone appear adequate for prevention of late anemia in most premature infants receiving diets of superior nutritional quality.

Seitelberger's Spastic Amaurotic Axonal Idiocy: A Report of a Case in a 9-Year-Old Boy with Comment on Visceral Manifestations. H. Nakai, B. H. Landing, and W. K. Schubert. Pediatrics 25:441-449 (March) 1960 [Springfield, Ill.].

The authors report the clinical and pathological findings of a 9½-year-old boy who had hypoplastic anemia between the ages of 8 and 26 months, and in whom later neurological manifestations developed with cerebellar and brain stem dysfunction. At autopsy the central nervous system showed a pattern of lesions, such as deposits of chromolipid pigment in basal nuclei, brain stem degeneration and gliosis of the dorsal portions of the brain stem and spinal cord, and formation of rounded or oval hyaline masses, apparently from axons of nerve cells. The dorsal horns of the gray matter of the cervical cord and the dorsolateral portion of the medulla and pons were markedly swollen by astrocytosis and microgliosis. Although none of these lesions could be considered pathognomonic, their occurrence in combination, with repetitive patterns of distribution, appeared to constitute a neuropathological entity, which the authors named "spastic amaurotic axonal idiocy," originally described by Seitelberger. The patient reported is apparently the first male in whom this rare familial disease has been recognized. He also had severe testicular atrophy, and nodular alteration of the adrenal cortex. The kidneys showed diffuse cortical interstitial fibrosis associated with patches of chronic inflammation and more marked interstitial scarring. Many tubules and glomeruli had thickened capsular membranes, and several distal convoluted tubules and loops of Henle contained casts. Many loops of Henle also showed brown granular pigment in tubular cytoplasm similar to that found in the brain. Either the renal or the adrenal lesions—very possibly both—can be considered responsible for the severe hypochloremia which marked the terminal illness.

The presence of chromolipid pigment in the renal tubular cells suggests that kidney biopsy or examination of the urinary sediment might be of value in the diagnosis of this disease. It will be necessary, however, to study more such patients to establish a definite connection between the deposits of pigment in the kidneys and spastic amaurotic axonal idiocy, and to prove the diagnostic reliability of kidney biopsy and of examination of the urinary sediment.

Conservative Management of Acute Renal Failure. S. A. Kaplan, J. Strauss, and A. M. Yoceoglu. Pediatrics 25:409-418 (March) 1960 [Springfield, Ill.].

Conservative treatment was used in 3 children with acute renal failure. There were 2 boys and 1 girl, ranging in age from 7 to 11 years. One patient died, but the other 2 completely recovered. It appears that in the early stages of renal failure the voided urine is iso-osmotic with plasma, and may represent unmodified fluid from the proximal tubules. Cardiac failure associated with hyperpotassemia or the administration of excessive quantities of fluid is the most frequent cause of death in acute renal failure. The authors suggest that the amount of fluid administered to patients with acute renal failure should be calculated to equal only the insensible water loss plus the volume of urine voided over the previous 24 hours. It is best to prevent acidosis by giving restricted quantities of sodium lactate immediately at the onset of the disease. The importance of weighing the patient every 24 hours is stressed in order to gauge if an excess of fluid and electrolytes has been administered to the patient. Hyperpotassemia should be treated with potassium exchange resins. It is advisable to administer calcium gluconate by mouth in case of hypocalcemia. Hyperphosphatemia is most effectively reduced by the oral administration of aluminum hydroxide gel. The potential usefulness of the intravenous administration of fat emulsions in patients with acute renal failure is emphasized to provide for adequate caloric intake. It is necessary to observe the patient carefully and to supervise the treatment even after the diuretic phase has set in, since manifestations of impaired renal function will persist for several days.

Mitral Atresia with Normal Aortic Valve: Report of 11 Cases and Review of the Literature. D. C. Watson, R. D. Rowe, P. E. Conen, and J. W. A. Duckworth. Pediatrics 25:450-466 (March) 1960 [Springfield, Ill.].

The authors report on a group of 11 infants and children with mitral atresia in whom a normal aortic valve was found at autopsy (Hospital for Sick Children, Toronto). The patients died between the ages of 1 day and 5 years. The records of 41 such cases reported in the literature were also reviewed. The average survival was 6 months. The general symptoms were cyanosis, dyspnea and physical retardation, usually accentuated 2nd heart sounds in the pulmonary area, and single and nonspecific murmurs. Congestive heart failure was frequent, and coarctation not uncommon. On the basis of history and physical examination, this malformation closely resembled a number of congenital cardiac defects. The roentgenograms usually visualized a large heart. Right ventricular hypertrophy with a QR pattern in the right precordial leads was a fairly consistent electrocardiographic finding. While this feature is not specific, it should prove to be a useful diagnostic aid in mitral atresia. Angiocardiograms showed a large right atrium and ventricle, and simultaneous filling of both great vessels, and also demonstrated pulmonary stenosis and transposition of the great vessels when present. Cardiac catheterization showed a rise in blood oxygen saturation in the right atrium, and systemic levels of systolic pressure in the right ventricle. Cardiac catheterization and angiography are necessary for final clarification of the disease.

Autopsy performed on all the children revealed a normal aortic valve; but the left atrium was small, and usually communicated with the larger right atrium by an atrial defect. Anomalies of the venous return were common. The right ventricle was large, and the left ventricle was either small, rudimentary, or absent. Pulmonary stenosis or atresia was frequently associated with transposition of the great vessels. The ductus arteriosus was usually patent, and preductal coarctation was common. Mitral atresia was associated with major extracardiac defects, especially with asplenia, in nearly half of the children. The microscopic appearance of the pulmonary arteries was abnormal in some older children.

Medical management of this malformation was not attended with success; also, all those with pulmonary stenosis, in whom shunt operations were performed, died either during or shortly after the intervention. At present the importance of the defect lies in its differentiation from potentially operable lesions, and in giving an accurate prognosis to the parents of affected children.

Long-Term Prognosis of the Nephrotic Syndrome in the Child: A Report on 193 Observations. R. Debré, J. Marie, P. Royer, and others. Semaine hôp. Paris 36:531-544 (Feb. 24) 1960 (In French) [Paris].

A study of 193 children with the idiopathic nephrotic syndrome is reported, 174 of them having been observed over a period ranging from 1 to 30 years. Depending on the treatment received, the 193 patients in this study were divided into 4 groups. The 1st group was composed of 34 children, 24 male and 10 female, who were seen between 1927 and 1944 and were treated before antibiotics became available. The 2nd group was composed of 36 children, 21 male and 15 female, who were treated with antibiotics. The 3rd group was composed of 68 children, 41 male and 27 female, who received antibiotics and short courses (8 to 15 days) of ACTH or cortisone between 1951 and 1955. The 4th group consisted of the remainder of the patients, but, on an average, 2 patients out of each group of 5 could not be followed; therefore, only 53 children were taken into consideration; these children were treated with antibiotics and long, but discontinuous, courses of ACTH, cortisone, or prednisone. In the 1st group 28 children were followed; 19 of them died, 8 recovered, and 1 suffered from sequelae. In the 2nd group 35 children were followed; 14 died, 18 recovered, and 3 suffered from sequelae. In the 3rd group 58 children were followed; 19 died, 31 recovered, and 8 suffered from sequelae. In the 4th group 30 children were followed; 5 died, 19 recovered, and 6 suffered from sequelae. The authors point out that the beneficial effect of antibiotics is evident in the data reported. Infection was responsible for 8 deaths in the 1st group, for 4 in the 2nd group, for 1 in the 3rd group, and for none in the 4th group.

The effect that corticotherapy had on the incidence of mortality due to renal insufficiency is hard to determine. Short courses of corticotherapy seem to have had no beneficial effect, since the mortality due to renal insufficiency increased from 10 (28%) in group 2 to 18 (31%) in group 3. It is also difficult to assess the effect of long courses, since no sufficient time has passed for an adequate follow-up evaluation in patients in whom the treatment with corticosteroids was discontinued, and a considerable number of patients are still under treatment at the time this report has been written.

Rubella as a Cause of Thrombocytopenic Purpura. A. W. Ferguson. Pediatrics 25:400-408 (March) 1960 [Springfield, Ill.].

The author reports a 3-year-old girl and a 7-year-old boy who were admitted to the Royal Hospital for Sick Children, in Edinburgh, because thrombocytopenic purpura occurred in both after rubella. A third child, a 7-year-old boy, is also described in whom thrombocytopenic purpura may have been secondary to a modified rubella infection. The serum of 2 of the children appeared to contain platelet agglutinins. The author reviews 16 other cases of thrombocytopenic purpura following rubella cited in the literature. Some clinical and pathological aspects of acute thrombocytopenic purpura in childhood are discussed, and it is suggested that infections mild enough to pass unrecognized, such as rubella, may precipitate the disease more frequently than is suspected.

OPHTHALMOLOGY

Corneal Lenses in Ophthalmic Practice. H. Agatston, A. H. Barnert, and M. Feldstein. Am. J. Ophth. 49:277-286 (Feb.) 1960 [Chicago].

The authors discuss the role of the ophthalmologist as a consultant, when the patient asks to be referred to a contact lens company or to a technician for fitting. The ophthalmologist is also often asked to perform a routine examination before fitting is begun, and after fitting by a technician. The authors define a corneal lens as one which fits over the cornea alone and not over the sclera; this includes lenses of varying sizes, shapes, and details of construction, such as the microlens, the contour lens, and many others, as well as the somewhat larger tuohy-type corneal lens. In contrast, a scleral lens has a corneal part, for optical purposes, and a part which rests on the sclera. In fitting a contact lens, the criteria for proper fit are (1) absence of damage to the cornea, and (2) the comfort of the patient, comfort including absence of symptoms and proper correction of the refractive error. In the discussion of the fit and the refraction, it is pointed out that fit is mainly concerned with the looseness or tightness of the lens, and this, in turn, depends on (1) the back surface or base curve, (2) the over-all size of the lens, called diameter, and (3) the amount and character of the bevel, if any. The refraction of the lens is determined by the power of the contact lens itself and also by its relation to the cornea, since this forms a so-called lacrimal lens which affects the refraction of the lens-eye combination.

Advantages of contact lenses over conventional spectacles are as follows: 1. There are cosmetic and psychological advantages, increase in the field of vision in high-refractive error and in aphakia, and better visual acuity in patients with irregular astigmatism, keratoconus, and refractive errors in the presence of nystagmus. 2. Less aniseikonia results in correction of monocular aphakia. 3. Magnification in myopia of moderate and high degree is an optical advantage. 4. There is no fogging of the lenses by mist, rain, snow, mud, or dust, and there is a safety factor compared with eyeglasses. Contact lenses are contraindicated in patients with epiphora; with excessive dryness of the eye due to such conditions as vitamin A deficiency, Sjøgren's syndrome, or pemphigus; with ocular infections or allergies; with local neoplasms; with degenerations of the cornea; with corneal edema; with a high degree of lenticular astigmatism; with severe exophthalmos; with thick or tight lids; with corneal insensitivity; and sometimes in the presence of presbyopia. Although hyperopes near the presbyopic age do well with contact lenses, older myopes who are comfortable reading with spectacles may be less comfortable with contact lenses.

Ultrasound in Ophthalmology. G. Baum and I. Greenwood. Am. J. Ophth. 49:249-261 (Feb.) 1960 [Chicago].

The authors discuss the application of sonar and radar techniques in ophthalmology. Sonar operates by sending forth repeated bursts of high-frequency sound, that is, greater than 20,000 cps. The sound waves strike the tissues and are reflected. The echoes are sequentially received and presented on the cathode-ray tube of a radar receiver. The physician observes the images of the interior structures of the body on the face of the tube. These images, or ultrasonograms, are cross sectional views, that is, they are compound coronal-sagittal sections of the eye and orbit, as viewed from an anteroposterior position. This equipment operates at 15 mc. The face of the tube may be photographed to obtain permanent records of particular views, such as are presented in this paper. Motion of the eyes is portrayed on the face of the cathode-ray tube much as motion of an actor is portrayed on a television set.

The authors show how analysis of the motion of the tissues may facilitate diagnosis on the basis of illustrative cases. One of the patients presented had a semiopaque cornea and a hemorrhage in both the anterior chamber and the vitreous of the eye. The interior of this eye could not be visualized with any existing ophthalmic instrument. Ultrasonic visualization demonstrated both the intraocular pathology and the orbital structures. The former proved to be a total retinal detachment, which contained within it the vitreous hemorrhage. Serial ultrasonography demonstrated the shift in position of the detached retina at different levels throughout the eye. The diagnosis and location of the retina were confirmed by the pathological sections. Tumors and vitreous hemorrhages also have been visualized by ultrasonography in the light-opaque eye.

Another major advantage of ultrasonic visualization is its ability to visualize and precisely locate radiolucent foreign bodies. Such localization may be performed through light-opaque mediums. Foreign bodies may readily be distinguished, even in the presence of amounts of blood which would render the fundus opaque to light. Radiopaque foreign bodies may also be visualized and localized without the use of external markers, which are ordinarily required for localization by roentgenologic films. The advantages of ultrasonic visualization over roentgenologic visualization are listed.

In discussing the orbital application of ultrasonography, the authors say that the optic nerve, check ligaments, and muscles have been visualized. Orbital tumors, cysts, and foreign bodies have also been demonstrated. Heretofore the location of orbital tumors could only be surmised. Roentgen-ray examination offered some assistance only if bone erosion occurred. This paper contains the first report of the ultrasonic visualization of a tumor and radiolucent foreign body within the orbit, and is a synopsis of all the forms of ultrasound which have been used in ophthalmology. Improved instrumentation and further clinical experience hold great promise for future diagnostic applications of the ultrasonic locator.

THERAPEUTICS

Use of Dexamethasone in Adrenal Cortex Inhibition Tests. J. Decourt, M. F. Jayle, J. P. Michard, and P. Mauvais. Semaine hôp. Paris 36:351-355 (Feb. 4) 1960 (In French) [Paris].

Given by mouth in a dose of 3 mg. per day, dexamethasone was found to have an almost complete inhibiting effect on the adrenal cortex. It seems that this dose should be adopted in the adult as a standard test for the study of hypercorticalism. The results obtained with this test in 2 patients wih congenital adrenal hyperplasia, in 8 with tardy virilism, in 2 with pituitary basophilism (Cushing's disease), and in 5 with adrenocortical obesity accompanied by hypercorticalism are reported. In the case of virilizing hypercorticalism it is pointed out that the inhibition test may enable differentiation to be made between simple hyperplasia and an adrenocortical tumor. The inhibition effect is very mild in the course of pituitary basophilism, while the test is quite effective in common obesity with hypercorticalism. Two comparative inhibition tests were made in 8 persons; in the 1st test dexamethasone was given in the dose indicated above, in the 2nd test the authors used delta hydrocortisone in a dose of 30 mg. for 5 days. The results obtained in the 1st test were much better than those obtained in the 2nd, especially with regard to the elimination of 17-ketosteroids and 17-hydroxy-corticosteroids. On the basis of a 6-month observation of 3 patients, the authors believe that prolonged treatment with a daily dose of 1 mg. of dexamethasone should provide adequate inhibition effect.

Complications on Peroral Treatment of Diabetes Mellitus with Sulfonyl Derivatives. K. Åstrom. Ugesk. laeger 122:10-18 (Jan. 7) 1960 (In Danish) [Copenhagen].

Peroral treatment of diabetes mellitus with sulfonylurea derivatives causes a number of side-effects, mostly not dangerous, but grave complications can occur. Tolbutamide is tolerated better than carbutamide, but the latter has a better antidiabetic effect. The most common side-effects with both substances are cutaneous changes of allergic kind seen mainly at the start of treatment, which usually disappear on discontinuation of the treatment or possibly on continuation of the treatment in the same or a smaller dose. Not a few cases of injury of the bone marrow have affected the myeloid system, leading to granulocytopenia. From April, 1956, to mid-June, 1959, 133 patients were treated with sulfonylurea derivatives, mainly carbutamide, in the Odense District and City Hospital, in Denmark. Cutaneous reactions were seen in 12 patients. Leukocyte and differential blood counts in 133 patients revealed a tendency to slight fall in the leukocyte count which later became normal. In 3 adults the granulocyte values were under 30%, the lowest count being 10%. In an infant given insulin and carbutamide, the granulocyte values fell to 5%. The thrombocytes, counted in 71 patients, showed a slight tendency to decrease during the treatment. In one patient tolbutamide caused grave thrombopenia with hemorrhagic diathesis, fever, joint disease, and impaired general condition; the patient recovered. No changes attributable to the treatment were seen in the red blood cell picture. Dyspeptic symptoms, mostly at the start of treatment, were observed in 10 patients treated with carbutamide and in 1 patient treated with tolbutamide. On long-term treatment the thrombocytes apparently tend to a steady, if slight, decrease, so that continued blood platelet control is desirable.

The Use of Antimalarial Drugs in Patients with Rheumatoid Arthritis. H. A. Souza, W. N. Vasquez, and J. Houli. Rev. brasil. med. 15:761-762 (Nov.) 1959 (In Portuguese) [Rio de Janeiro].

Sixty patients with rheumatoid arthritis were treated with antimalarial drugs for different periods of time. These patients were observed in 3 groups. Group 1 was composed of 10 patients who had been suffering from rheumatoid arthritis for from 15 days to 3 years. They were treated for longer than a year as outpatients, receiving first chloroquine phosphate and later hydroxychloroquine sulfate. At the end of 30 days the dose was decreased from 2 tablets to 1, or, if the patient's condition so required, it was increased to 3 or even 4 tablets The treatment was well tolerated in spite of initial anorexia and loss of weight. Therapeutic results were observed, on the average, at the end of 30 days, with relief of the pain, greater mobility, disappearance of local heat and redness, and of the edema. The treatment was interrupted for some patients in order to test the permanence of the results. These patients continued to be free from symptoms for 30 to 45 days. When the symptoms reappeared, the treatment was resumed, with the same initial favorable results.

Group 2 was composed of 20 patients who were observed for 6 months. Good results were obtained in 50% of this group under the same therapeutic orientation as in group 1. When a patient developed intolerance to chloroquine phosphate, this preparation was replaced by hydroxychloroquine, which was generally well tolerated. Group 3 was composed of 30 patients who had been observed for periods of 1 to 3 months when this article was written. The patients were tolerating the treatment well, with only mild reactions which did not require interruption of the therapy. The authors believe that the antimalarial drugs used in this study are effective in long-term treatment of rheumatoid arthritis, bringing the patients long remissions and, possibly, cure.

Experimental Treatment of Angina Pectoris with a New Active Principle Extracted from Ammi Visnaga (Visnadin) and Different from Khellin. M. Mouquin and C. Macrez. Presse méd. 68:257-258 (Feb. 13) 1960 (In French) [Paris].

Thirty patients with angina pectoris and coronary disease, who were under electrocardiographic surveillance as outpatients, were treated with Visnadin, a derivative of dihydrofurocoumarin and, therefore, different from khellin which is a furanochromone. Several of the patients had been hospitalized in the past because of myocardial infarction. The majority made regular use of trinitrin tablets. Visnadin was administered orally in daily doses of 2 to 6 tablets (25 or 50 mg.), which were alternated with a placebo. The therapy was well tolerated except by 5 patients who were over 65 years of age. Unfavorable reactions were nausea, vomiting, and vertigo in 3 patients, gastralgia in 1, and generalized pruritus in 1.

The results of the Visnadin therapy were evaluated in terms of the angina manifestations. Electrocardiographic control was not considered entirely reliable, since spontaneous changes take place in patients with coronary disease. Another criterion for evaluation was the amount of trinitrin still needed to prevent anginal attacks. The results were considered excellent in 7 patients who became entirely free from symptoms as long as they were given Visnadin. The most satisfactory results, though, were only palliative and temporary, and the symptoms reappeared if the treatment were suspended. Good results were obtained in 9 patients whose attacks were reduced in number to one-half or one-third, and whose daily dose of trinitrin could also be reduced. Four patients obtained only mediocre results, without any improvement over those obtained with other drugs. The authors believe that Visnadin, as a preparation of low toxicity, represents an additional asset in the treatment of coronary insufficiency, and that doses of between 0.05 and 0.30 Gm., given orally daily, are adequate in almost all cases.

Treatment of Pulmonary Tuberculosis: "Strong" Doses of Isoniazid. E. Bernard, A. P. Jarniou, L. Israel, M. Enjalbert, and C. Fabre. Presse méd. 68:209-210 (Feb. 6) 1960 (In French) [Paris].

Two groups of patients with pulmonary tuberculosis were treated during 3 months with different doses of isoniazid. An experimental group, composed of 114 patients chosen at random, received 15 mg. of isoniazid per kilogram of body weight, while a control group, composed of 90 patients also chosen at random, received 5 mg. per kilogram of body weight. In addition, the experimental group received an intramuscular injection of 200 mg. of pyridoxine (vitamin B_6) 3 times a week, and both groups received 15 Gm. of PAS daily in intravenous perfusion. The results were evaluated in terms of radiologic and bacteriological changes and were classified as very important, and moderate improvement; stationary aspects; and aggravation.

Radiographic and tomographic findings showed important and very important improvement in 50.8% of the high-dose group and in 38.8% of the regular-dose group. The advantages of the higher dose were visible at the end of 2 months of treatment and were more pronounced by the end of the 3rd month. The patients with cavitation profited from the high-dose treatment to a greater extent than the others. Bacteriological findings showed that the proportion of patients who remained positive for tubercle bacilli in the high-dose group (8 of every 45 patients) was lower than in the regular-dose group (11 of every 42 patients), a difference which represents a 35% superiority. Tolerance to the drug was satisfactory, with only one patient having to interrupt the treatment because of side-effects. Although the patients treated with high doses of isoniazid had also received pyridoxine as a prevention against unfavorable reaction, the authors now believe that this systematic preventive treatment is not always necessary. The administration of pyridoxine is recommended only for patients predisposed to nervous disorders.

PATHOLOGY

Staphylococcus Infections in Hospitals. C. W. Findlay Jr., B. A. Johnson, and L. Goode. Dis. Colon & Rectum 3:9-14 (Jan.-Feb.) 1960 [Philadelphia].

The authors collected data regarding the phage types of coagulase-positive staphylococci on the surgical service of the Presbyterian Hospital, New York. This type of research is an important method of studying the epidemiology of staphylococci. An attempt was made to determine the prevalence of certain phage types, especially type 80-81, in patients admitted with infections and in hospital-incurred infections. The occurrence of these types was also investigated in infections observed in outpatients. To study the possible routes of transmission, cultures were taken and typed from inpatients, personnel, the air of the wards, and from actual infections. The results showed that the incidence of the phage type 80-81 was less in patients seen in the hospital than in those seen in the outpatient departments. This was determined by studying the organisms causing axillary and breast infections during a period of 6 months. In another survey the organisms from all staphylococcic infections occurring in any one-month period were typed. Only one of the in-hospital infections was due to the 80-81 phage type, whereas almost one-third of the infections acquired before admission were caused by this type.

Sampling of the air of all wards on the surgical service at weekly intervals revealed that phage type 52A-79 was a common contaminant, while type 80-81 was rarely obtained. Cultures from infections in 31 nurses working in all parts of the hospitals were made and typed over a period of 7 months. Most of these infections occurred in the form of furuncles. Sixty-eight per cent of these infections were due to phage type 80-81, and most of the organisms were multiresistant to antibiotics. Cultures from the respiratory tracts and stools of ward patients yielded only a small percentage of strains of the 80-81 type. Only 16% of the postoperative wound infections that occurred on the surgical service between March and November, 1958, were due to type 80-81. During this period there were only 3 cases in which correlation could be detected between the environment and the development of infection. Phage type 80-81 was involved in these 3 cases. The much-publicized 80-81 type was just as common in outpatients as it was among those residing in the hospital. Many of these strains were sensitive to all antibiotics. This type apparently was more bothersome to the nursing personnel than to the ward patients. There was no evidence that these organisms were frequently transmitted by the air of the wards. Although the distribution of phage types may change from year to year, this method will be useful should infection problems arise, and it will also provide valuable data for retrospective evaluation.

Histological Aspects of the Auricular Appendix in Patients with Mitral Stenosis. L. V. Décourt, M. R. Montenegro, N. Sawaya, and R. Castiglioni. Rev. Hosp. clín. 14:389-396 (Nov.-Dec.) 1959 (In Portuguese) [São Paulo, Brazil].

Thirty-five patients suffering from pure mitral stenosis were selected from a series of 320 patients who underwent commissurotomy on the cardiologic service of the Hospital das Clinicas, University of São Paulo, for an investigation on the histological condition of the auricular appendix. These patients were selected on the basis of (1) a complete history of rheumatic background, and (2) absence of any clinical or laboratory findings suggestive of present rheumatic disease. The patients received premedication with benzathine penicillin in the dose of 1.2 million units a week. Eleven of them also received digitalis. Roentgenograms, electrocardiograms, and hemograms were obtained, as well as tests of erythrocyte sedimentation, C-reactive protein, total proteinemia, and protein flocculation. Three different sections were obtained from each surgical specimen, and the histological findings were classified according to the extension (diffuse or focal) and the intensity of the inflammation.

The histological examination of the auricular appendix specimens showed no inflammation in 8 patients, nonspecific inflammation in 6, and signs of active rheumatic disease in 21. Typical Aschoff bodies were found in specimens from patients with a negative history for rheumatic fever and from patients who had long been asymptomatic. Electrocardiographic abnormalities were observed in relation to P-R and Q-T intervals and were always associated with important histopathological findings. The authors believe that clinical and laboratory data are insufficient for the diagnosis of subclinical rheumatic fever, and recommend that alterations in P-R and Q-T intervals be more carefully investigated as diagnostic aids.

Relationship of Viruses to Malignant Disease: I. Tumor Induction by SE Polyoma Virus. E. A. Mirand, J. T. Grace, G. E. Moore, and D. Mount. A. M. A. Arch. Int. Med. 105:469-481 (March) 1960 [Chicago].

The authors performed tumor-producing experiments in mammals, including hamsters, mice, rats, rabbits, and monkeys, at the Roswell Park Memorial Institute in Buffalo. Tissue culture fluids containing the tumor-inducing agent (referred to by Stewart and Eddy as "SE polyoma virus"), usually obtained by inoculating Swiss mouse embryo tissue cultures with minces of polyoma-induced tumors from mice, hamsters, or rats, were the sources of tumor-producing material. The results showed that SE polyoma virus induced a wide spectrum of tumors in hamsters, mice, and rats. Age was an important factor in susceptibility to polyoma virus. Strain variations in susceptibility in mice were noted. Lymphatic leukemia along with parotid tumors developed within 4 months in newborn AKR/Sn mice in which polyoma virus had been injected. The virus was readily recovered in tissue culture from induced tumors. Induced tumors were grown on chick chorioallantoic membrane, and the virus was recovered in tissue culture from these egg tumors. The virus did not produce visible morphologic changes in the embryonated egg. A correlation between cytopathogenicity of the virus in tissue culture and tumor induction was seen. No relationship of hormonal factors to tumor induction was found. These virus-induced tumors were poorly transplantable; however, when transplantation was successful, the virus-induced tumors obeyed the genetic laws of transplantation. The presence of inapparent polyoma virus infection was observed in several mouse colonies at this institute.

Relationship of Viruses to Malignant Disease: II. Oncogenic Properties of Cell-Free Filtrates of Human Tumors. J. T. Grace Jr., E. A. Mirand, and D. T. Mount. A. M. A. Arch. Int. Med. 105:482-491 (March) 1960 [Chicago].

The fact that viruses can cause cancer in a wide variety of animals was established again in the preceding paper. Consequently, the authors investigated a large number of human tumors, obtained at surgery or autopsy, for the presence of oncogenic viruses. Extracts of these tumors were inoculated into a variety of established tissue cultures in an effort to grow potential oncogenic viruses in vitro. Fluids from these tissue cultures were injected into newborn Swiss ICR (Ha) mice and hamsters to assess their tumor-producing properties. Similar extracts were injected directly into newborn animals with or without preceding filtration of the extracts through a bacterial filter. Malignant tissues from 47 patients with acute leukemia, chronic leukemia, Hodgkin's disease, malignant melanoma, soft tissue sarcoma, neuroblastoma, nephroblastoma, osteogenic sarcoma, lymphosarcoma, and gastrointestinal tumors were studied by these methods.

The results showed that no tumors have appeared in animals receiving injections of the tissue culture preparations. Many tumors have appeared in mice which were given direct injections of supernates and/or filtrates of human tumors. Most of the animal tumors were carcinomas of the breast, and the latent periods varied from 3 to 9 months. The incidence of breast tumors was highest in pregnant mice. There was no correlation between the type of human tumors employed and the type of tumors appearing in mice. Material from human leukemic tissues was associated with the greatest number of animal tumors. No tumors occurred during this time in 3 large groups of contratest animals. The possibility that oncogenic viruses are implicated is being investigated. Serologic studies showed that the polyoma mouse-tumor virus was not involved.

Bactericidal Action of Penicillin and Tetracycline Against Gram-Positive Cocci in Broth and in Blood Clots, with a Few Observations Concerning "Persisters." M. Hamburger and J. Carleton. A. M. A. Arch. Int. Med. 105:372-382 (March) 1960 [Chicago].

The authors studied the rate of bactericidal action of penicillin and tetracycline against bacteria grown in broth or seeded in blood clots suspended in broth. The 4 microbic species studied were Streptococcus viridans, Staphylococcus aureus, Staph. albus, and Diplococcus pneumoniae, type 2, which had been recovered from patients with bacterial endocarditis. Special attention was accorded to the complete sterilization of the broth culture or the clot. Because in infections like bacterial endocarditis the presence of small numbers of "persisters" (bacteria which remain viable in antibiotic-containing environments after most of the siblings have been killed, but which retain their in vitro sensitivity to the same antibiotic) may pave the way for relapse, experiments were continued, when possible, until cultures were sterile. This end-point could be established with confidence in the case of only 2 antibiotics, penicillin and tetracycline.

Two or 3 times as many days were required to kill streptococci of the viridans group seeded in clots as when the same strains were grown in broth. Increasing the concentration of penicillin 100 times did not lead to more rapid elimination of the "persisters." However, more rapid killing was effected in both clots and broth when the inoculum of streptococci was reduced 1,000-fold. A large inoculum of a penicillin-sensitive strain of Staph. aureus in broth was rapidly reduced in numbers by either high or low concentration of penicillin, though a few "persisters" survived for a total of 5 to 9 days. The rate of elimination of these "persisters" was about the same for both concentrations of antibiotic. When the staphylococci were seeded in clots, penicillin reduced the bacterial population more slowly. During the first 9 days the rate of bactericidal action was not significantly different with high or low concentration of antibiotic. After this period no staphylococci persisted in clots incubated with the higher concentration of penicillin, but were found in small but significant numbers as long as the 37th day of incubation with the lower concentration.

Clots seeded with Staph. aureus and incubated in penicillin-free broth were divided at the end of 4 days. One-half was cultured quantitatively; the other half was transferred to broth containing no penicillin, 0.5 mcg. of penicillin per milliliter, or 50 mcg. of penicillin per milliliter. After a week's further incubation, staphylococci in the half clots transferred to penicillin-free broth increased their numbers by 10-fold to 100-fold. In the clots transferred to broth containing 0.5 mcg. of penicillin per milliliter, the staphylococcic population was reduced about 10,000-fold. When the broth contained 50 mcg. of penicillin per milliliter, the reduction was more than one-million-fold. Similar clots were initially incubated in broth containing 0.5 mcg. of penicillin per milliliter. After 4 days the staphylococcic population fell 100-fold. When these clots were divided and reincubated for a week, the "partially poisoned" staphylococci in the halves transferred to penicillin-free broth increased in numbers, whereas the half-clots transferred to broth containing penicillin were sterile or nearly sterile.

Type 2 diplococci survived as long as 13 days when they were seeded in blood clots and incubated in penicillin-free broth. When the broth contained 0.5 mcg. or 50 mcg. of penicillin per milliliter, all clots cultured after the 4th day were sterile. No "persisters" were observed.

Tetracycline was more effective against staphylococci in broth than in clots in 2 important respects: 1. The bactericidal rate was faster in broth than in clots. 2. The minimal concentration of this antibiotic necessary to eradicate a large inoculum of staphylococci from a clot was about 10 times that which sterilized a broth culture. In both broth and clots the bactericidal effect was greater either when the concentration of the drug was higher or when the inoculum of staphylococci was smaller.

Cancer Cells in Gastric Rinse Water: Chymotrypsin Method. B. Bach-Nielsen and E. Amdrup. Ugesk. laeger 122:40-43 (Jan. 14) 1960 (In Danish) [Copenhagen].

Sixty patients observed because of gastric symptoms were examined by exfoliative gastric cytology. In 45 patients the diagnosis was verified histologically. Fourteen patients had cancer of the stomach; in 11 of these, typical cancer cells had been raised on rinsing the stomach with chymotrypsin solution, in 2 patients definite diagnosis could not be made, and in 1 patient cancer cells could not be raised. In 31 patients benign gastric disease was verified. Gastric cytological examination gave 3 false-positive answers, 2 of them due to inexperience on the part of the examiners. Cytological examination of patients with gastric diseases can undoubtedly become a useful supplement to the methods of examination usually employed.

The Effect of the Intestinal Flora on the Growth Rate of Mice, and on Their Susceptibility to Experimental Infections. R. J. Dubos and R. W. Schaedler. J. Exper. Med. 111:407-417 (March) 1960 [New York].

Mice delivered with sterile technique by cesarean section were used to develop a new mouse colony, which has been maintained in an environment protected from contact with common mouse pathogens, but not in the germ-free state. These mice, designated as Nelson-Collins-Swiss (NCS), were compared with animals of the same sex and age coming from the parent colony maintained under ordinary conditions. The NCS mice grew more rapidly than ordinary mice on complete diets; moreover, they continued to gain weight, although at a slower rate, when fed deficient diets which caused ordinary mice to stop growing or to lose weight. The NCS mice proved much more susceptible than ordinary mice to experimental infections caused by Klebsiella pneumoniae, type C, staphylococci, and tubercle bacilli. In contrast, they were much more resistant than ordinary mice to the lethal effect of large doses of endotoxins. However, they responded to injection of minute amounts of these endotoxins by a marked increase in susceptibility to staphylococcic infection.

Bacteriological studies revealed striking qualitative differences between the intestinal flora of the NCS mice and ordinary mice. When NCS mice were contaminated, either by contact or by feeding, with a strain of Escherichia coli recovered from the intestine of ordinary mice, they acquired the characteristics of these latter animals with regard to weight gain on various diets and response to bacterial pathogens and endotoxins. NCS mice have been found well suited to the study of several nutritional, bacteriological, and immunological problems, and it appears that their production on a large scale will not present unsurmountable difficulties.

An Evaluation of Serum Transaminase in the Jaundice States. H. J. Sacks and G. F. Lanchantin. Am. J. Clin. Path. 33:97-108 (Feb.) 1960 [Baltimore].

Since it was demonstrated that the serum glutamic oxalacetic transaminase (SGO-T) increased after myocardial infarction, elevated SGO-T values have been reported in 6 groups of illnesses. These include injury to skeletal muscle, hepatobiliary disease, extensive damage to the brain, hemolytic anemia, certain chemical and drug intoxications, and some instances of pulmonary infarction. This paper deals with a study of the level of serum transaminase in 120 patients with jaundice of varying etiology, who were admitted to Cedars of Lebanon Hospital and Clinic in Los Angeles from November, 1956, to January, 1959. Diagnosis was occasionally by biopsy, but it was chiefly clinical in the medical cases of jaundice; in the duct obstruction cases it was generally made at surgery or autopsy. The SGO-T levels were determined serially in most of these patients, and to a less extent analyses were made of the serum glutamic pyruvic transaminase (SGP-T). During the early phase of the investigation the SGO-T values were determined spectrometrically, but later mostly colorimetrically. When it was found that the colorimetric values were consistently lower than those obtained by spectrophotometric analysis, the authors plotted the results of the 2 methods of analysis against each other, and thus derived the factor 1.38, that is, the colorimetric result was multiplied by 1.38 in order to arrive at the approximate spectrophotometric equivalent, and the spectrophotometric value was divided by 1.38 to find the equivalent colorimetric value. With regard to the SGP-T values, however, the conversion factor is 2.

Discussing the results, the authors say that the SGO-T level among 30 patients with viral hepatitis exceeded 500 units in 21 instances. There was no statistical difference between the levels in serum hepatitis (11 cases) and infectious hepatitis (19 cases). There were 2 patients with less than 300 units, but inasmuch as these were convalescing at the time of study, the peak SGO-T value may have been missed. The highest value in this series was 10,000 units. In commenting on the course of serum hepatitis in 2 patients, in whom the transaminase values showed essentially the same behavior as in patients with infectious hepatitis, the authors emphasize the early striking rise of SGO-T values prior to the onset of icterus. Studies illustrated the importance of obtaining the SGO-T value at the ascendancy of the illness, prior to the peak of the jaundice. The subsequent course of both patients is also typical in that, as the bilirubin continued to decrease in concentration, the SGO-T and SGP-T levels fell in parallel manner.

In the concluding summary the authors state that SGO-T values of 1,000 units or more per milliliter were observed to be diagnostic of hepatocellular damage. Values exceeding 500 units seem to exclude surgical obstructive jaundice, and such levels were observed in most instances of viral hepatitis, in hepatitis associated with the use of iproniazid (Marsilid), and in massive hepatic necrosis. The SGO-T levels exceeded 500 units also in 3 patients with carcinoma of the liver and in 3 with pancreatitis.

SGO-T values of less than 500 units per milliliter were not specific for the type of jaundice present. In this range, SGO-T: bilirubin ratios greater than 1:40 presumptively exclude duct obstruction; ratios less than 1:40 presumptively exclude hepatitis. In the presence of jaundice and levels for SGO-T in excess of 500 units, data on SGP-T do not provide additional information. With SGO-T values of less than 500 units, SGP-T may be of help in excluding hepatitis from consideration, if the SGO-T:SGP-T ratio exceeds 1:3.18. On the other hand, the ratio is not suitable for distinguishing duct obstruction from cirrhosis.

A New Method of Preservation of Vessels by Embedding the Specimens in a Plastic Material Which Hardens Rapidly. G. Carstensen. Chirurg 31:49-52 (Feb.) 1960 (In German) [Berlin].

Eighty-seven thoracic or abdominal aortas obtained from dogs within 2 hours after their exsanguination were embedded in a thermoplastic substance produced by polymerization; the basic material is the methyl ester of methacrylic acid. The polymerization of the rapidly hardening substance takes place at room temperature while heat is liberated. The monomer methyl methacrylate is called Palacos. With the aid of an electrical oscillation-saw and a chisel, the plastic material can be removed within 3 minutes before the specimen is used for grafting. The plastic material is hydrophobic and does not unite with the vessel. After the removal of the plastic material, the specimen is placed in a sterile sodium chloride solution to which an antibiotic and heparin have been added.

Transplants of aortas, which had been preserved by this technique, were made into the abdominal aortas of 14 dogs. In some of the animals the aorta was replaced from closely below the branching off of the left renal artery up to the trifurcation (in the canine aorta). Thirteen of the 14 animals survived this surgical intervention with a patent transplant. One animal died of cardiac insufficiency with a resulting thrombosis of the graft. The maximum duration of preservation of the transplanted vessels was 75 days. The longest survival time after the transplantation was about 140 days. Completely patent vessels were found in the killed animals. These findings show that a homologous vascular transplantation is possible after preservation of the vessels by embedding them in a rapidly hardening plastic material.

Splenomegalic Cirrhoses. E. C. Pascual. Rev. españ. enferm. ap. digest. 18:1354-1449 (Nov.) 1959 (In Spanish) [Madrid].

The author reviews 70 cases of splenomegalic cirrhosis mainly from the etiological viewpoint. The patients' ages ranged from 8 to 67 years. The etiological factor was a viral infection in most of the 70 patients studied; bacterial infections or intoxications were observed in a few exceptional cases. Clinically, the hepatosplenic syndrome manifested as chronic congestive splenomegaly (Banti's disease), associated with hypersplenism; this was almost always characterized by hemolytic anemia with splenomegaly of an autoimmunological origin, with leukopenia, thrombopenia with purpura, and a chronic hepatic condition which developed into cirrhosis.

Anatomicopathologically, there were outstanding signs of hyperfunction of the reticuloendothelial system, together with the most varied lesions of the hepatosplenic vascular system. These lesions were often of the lupoid vasculitis type, always associated with hyperglobulinemia, therefore, with complete and incomplete antibodies and, above all, with autoagglutinins. In most patients these reticulohistiocytic lesions spread beyond the hepatosplenic area, with gamma-globulin accumulation in the renal glomeruli and in serous endothelium, causing hyperplastic and exudative reactions. The reticuloendothelial reactions were often followed by collagen hyperproduction with hyperplasia and hyperfunction of fibroblasts and fibrocytes, involving the endocrine glands and thus resembling Selye's allergic-rheumatic reaction.

The author believes that the current immunological theories are insufficient to account for the characteristic features of splenomegalic cirrhosis. It is his opinion that the clonal-selection theory, proposed by Jerne and applied by Burnet and others, offers a better explanation. According to this theory, movable colonies of mesenchymal cells which are present mainly in the spleen, but also in the liver, become pathological or forbidden clones as a result of mutations. A defective hemostasis allows these clones to persist after the embryonic stage, and the patient develops some form of autoimmunological disease. The pathological clones are the source of autoantibodies found in the plasma of cirrhotic patients. The author believes that splenomegalic cirrhosis presents one of the most intriguing problems in modern immunology, and that the theory of autoimmunological reaction will be one of the main objectives in medicine for the next 10 years, with many fruitful therapeutic applications.

RADIOLOGY

Hiatal Hernia: Roentgen Incidence and Diagnosis.

G. N. Stein and A. Finkelstein. Am. J. Digest. Dis. 5:77-87 (Feb.) 1960 [New York].

The authors made a study on 100 consecutive patients, referred to the radiology department of the Graduate Hospital of the University of Pennsylvania, Philadelphia, for roentgenologic study of the upper intestinal tract and diagnosis of hiatal hernia. The examination of the cardioesophageal junction for hiatal hernia requires the patient to be in the recumbent position, prone-oblique, the right arm at his right side, the left arm resting on the table above his head. The left knee and hip are flexed, so that the side of the body is elevated between 10 and 30 degrees, and the head is turned to the left. The examination must be made while the patient is swallowing the contrast material. The fluoroscopist notes how long a time lapse occurs between initiation of the swallowing act and the arrival of the bolus in the critical area. The authors do not believe the examination is diagnostic if films are exposed after the main bolus has passed. Only large hernias are shown in this manner. The patient should suck a large mouthful of contrast material through a straw and keep it in his mouth until the examiner is ready to expose the film.

The examination must consist of multiple exposures of the cardioesophageal region made in various phases of respiration. The authors generally use a serialogram, permitting 4 Bucky exposures on one 10-by-12-in. film. After the patient has swallowed the barium mixture, the 1st and 3rd exposures are made in deep inspiration to take advantage of the closing mechanism of the lower esophagus. The alternate exposures are made during cessation of respiration about midway between normal inspiration and expiration, because occasionally hernias are better demonstrated in this stage. The routine examination consists of at least 2 sets of such serialographic exposures (8 exposures), occasionally supplemented by spot films of the cardioesophageal junction.

With this technique of examination, 50 hiatal hernias were detected in the 100 patients who ranged in age from 20 to 85 years. Although the incidence was higher in patients over the age of 40, even in those under 40 it was 34.7%. The authors feel that this high incidence is attributable in part to the technique of the examination and in part to the rather broad definition of the term "hiatal hernia." The roentgenologic diagnosis of hiatal hernia is usually of clinical importance only insofar as it can be correlated with the patient's symptoms.

Abnormal Electrocardiograms in Apparently Healthy People: I. Long Term Follow-up Study.

F. A. L. Mathewson and G. S. Varnam. Circulation 21:196-203 (Feb.) 1960 [New York].

A long-term study of roentgenologic findings in 3,983 apparently healthy military and civilian pilots was made over a period of approximately 18 years. Contacts were renewed annually by means of a return post card, supplemented by periodic medical and electrocardiographic examinations. All the subjects were fit for flying duties when the initial electrocardiograms were recorded. These electrocardiograms, taken from the early years of World War II until 1948, were normal in 3,832 subjects, but at the last examination 41 of them were questionable and 44 were abnormal. In the entire series the electrocardiograms of 151 persons were abnormal on entry. Myocardial disease developed in 27 (0.7%) of the 3,832 normal subjects and in 5 (3.3%) of those with abnormal electrocardiograms on entry.

Partial heart block, paroxysmal tachycardia, shifts in the RS-T segment, and primary T-wave changes tended to occur intermittently, while QRS voltage changes, pathological Q waves, complete heart block, Wolff-Parkinson-White configuration, and bundle-branch block usually remained constant once they appeared. At the observed ages and durations the subjects whose electrocardiograms exhibited partial heart block, Wolff-Parkinson-White configuration, and right bundle-branch block have remained, with one exception, in apparent good health. Low QRS voltage, high QRS voltage, and primary T-wave changes, with or without a shift in the RS-T segment, were the only abnormal electrocardiographic components that preceded the onset of myocardial disease. However, these abnormalities, being present in many other instances, were not followed by onset of a clinical disease. During the follow-up period 83 deaths were recorded, of which 7 were related to myocardial disease.

PHYSIOLOGY

Effects of a Short Period of Training of Varying Severity on Some Measurements of Physical Fitness. J. V. G. A. Durnin, J. M. Brockway, and H. W. Witcher. J. Appl. Physiol. 15:161-165 (Jan.) 1960 [Washington, D. C.].

The authors subjected 44 physically untrained men, 41 between the ages of 18 and 22 years and 3 slightly older, who were in the Royal Air Force, to varying degrees of exercise over a 10-day period in an attempt to measure the effect of these exercises on their physical fitness. The men were divided into 4 groups.. One group, consisting of 8 men, served as controls, and the members of this group did only a minimum amount of exercise. The 12 men in each of the other 3 groups walked 6 miles (10 km.), 12 miles (20 km.), and 18 miles (30 km.), respectively, daily. Fitness was assessed by measurements of pulmonary ventilation, oxygen extraction, oxygen consumption, and heart rate during a standardized physical test on the treadmill. The test was done before, during, and after the period of training. The group of men walking 12 miles daily showed the most marked improvement in fitness, with a significant lowering of pulmonary ventilation, oxygen consumption, and heart rate during the test. Walking 12 miles daily is an exercise which requires no skill or apparatus and could be applied to large groups, such as army recruits, in whom an increase in physical fitness might be needed at short notice.

Lung Volumes of Singers. S. S. Heller, W. R. Hicks, and W. S. Root. J. Appl. Physiol. 15:40-42 (Jan.) 1960 [Washington, D. C.].

The authors made lung volume determinations, including tidal volume, inspiratory capacity, inspiratory reserve volume, expiratory reserve volume, vital capacity, maximum breathing capacity, functional residual capacity, residual volume, and total lung capacity, on 16 professional singers and on 21 persons who had had no professional vocal training. Regardless of whether the measurements were made in recumbent or standing positions, and in terms of the various divisions of lung volume, no significant differences were found between the 2 groups which could not be explained on the basis of age, size, or errors involved in making the measurements.

PUBLIC HEALTH

Intradermal Vaccination in Healthy Adults with Type A Asian Strain Influenza Vaccine. M. L. Candler, G. R. Cooper, U. P. Kokko, and others. Proc. Soc. Exper. Biol. & Med. 103:151-154 (Jan.) 1960 [Utica, N. Y.].

The intradermal route for the administration of influenza vaccine, Asian strain, type A, was employed widely in the fall of 1957 when the demand for this vaccine exceeded the supply. The studies described were carried out to determine the relative efficacy of various doses of vaccine in producing measurable immune responses. When the investigation was begun in September, 1957, no clinical influenza had been reported in the study area. The vaccine used was a single lot of commercially prepared monovalent, Asian A influenza vaccine which contained 1,000 chicken cell agglutination (CCA) units per milliliter. To administer different amounts of the vaccine in the same volume, it was diluted with pyrogen-free isotonic sodium chloride solution to make 4 concentrations containing 12.5, 25, 50, and 100 CCA units in 0.1 ml.

A total of 242 volunteers (civilian employees of the Army Corps of Engineers) in Atlanta, Ga., were randomly assigned to 5 groups which received 0.1 ml. of Asian A influenza vaccine intradermally in the volar surface of the forearm. Groups 1, 2, 3, and 4 received 12.5, 25, 50, and 100 CCA units, respectively, and group 5 also received 100 units. Groups 1 to 4 received a second dose of vaccine after a 2-week interval; group 5 received only one injection. In October, 1958, 53 weeks after the program had begun, a booster vaccination was administered to 79 volunteers. The booster dose for each was the same size as the first dose. Venous blood was collected from all volunteers prior to administration of the 1st injection of vaccine (week 0), prior to the 2nd dose (week 2), and again 2 weeks later (week 4). Additional blood, specimens were obtained from 75 subjects 16 weeks after the 1st injection. During the booster phase of the program, blood specimens were collected from all returning subjects just prior to the vaccine injection (week 53) and again 2 weeks later (week 55).

The antibodies detectable in the volunteers 2 weeks after the 2nd injection varied with dose from 44 to 70%, with titers 1:40 or greater. The intradermal booster immunization, administered 53 weeks after the 1st vaccination, induced marked rises in titers which were also related to dose. The geometric mean titers ranged from 1:21 to 1:51 within 2 weks after the 2nd injections of vaccine, and rose to 1:51 to 1:211 within 2 weeks after the booster injection. Two separate injections of 50 CCA units resulted in better antibody responses than single injections of 100 CCA units. Even the response to 2 injections of 12.5 CCA units was as good as the response to single doses 4 times as large. Systemic and local reactions increased with unit dose of vaccine, but no serious reactions occurred with the lot of vaccine used throughout this study.

A Trial of Bacterial Vaccines for the Common Cold in the Royal Air Force. D. L. Miller, J. C. McDonald, R. E. O. Williams, and J. S. Wilson. Lancet 1:358-360 (Feb. 13) 1960 [London].

The authors report a controlled trial of bacterial vaccines among a total of 293 flying personnel of the Royal Air Force. The men were divided into 3 groups and were given an autogenous vaccine, a pool vaccine, and a phenol saline solution, respectively, in a course of 3 initial doses in October, 1958, and a reinforcing dose in January, 1959. The volunteers were observed until the end of March, 1959, and records were made of all their respiratory infections during this time. The total incidence and severity of the respiratory disease rate in the 3 groups were about the same. It was clear from the results that autogenous bacterial vaccines are unlikely to have any practical application in dealing with the problem of the common cold among the flying personnel of the Royal Air Force. There was, however, a statistically significant reduction in the incidence of illness among those who received autogenous vaccines between the 3rd and 6th weeks after the 3rd and reinforcing doses. Autogenous bacterial vaccines, perhaps in greater dosage, may therefore merit further investigation among less healthy persons.

Analysis of 247 Consultations for Poisonings in Wisconsin. W. T. Bruns and J. T. Azzam. Wisconsin M. J. 59:143-144 (Feb.) 1960 [Madison].

The poison information center at the University Hospitals in Madison, Wis., operates predominantly as a consultation center, from which practicing physicians can obtain information related to intoxication problems. The authors evaluated 247 inquiries concerning 253 patients. Of these inquiries, 15% concerned infants in the 2nd year of life, and 51% concerned children between 2 and 4 years of age. There was a slight predominance of boys in the preschool age group; only girls were reported for the age range between 10 and 18 years. Information regarding the reason for and type of poison ingested in the older age group indicated that these were mostly abortive suicide attempts.

Physicians usually do not inquire regarding poisons that are familiar to them, and so this group of patients included few cases of poisoning with aspirin or the barbiturates. In only 22 instances were consultations requested which stated specifically the involved chemical substance. In the remaining 225 calls the chemical composition was either completely unknown or the physician wished to have his information confirmed. Most of the inquiries were concerned with the ingestion of household products, chiefly hydrocarbons, corrosives, bleaches, antiseptics, and pesticides. Drug-induced poisonings, regarding which inquiries were received, concerned mostly toxic drugs, tranquilizing agents, selenium sulfide, and salicylates. A follow-up inquiry was begun for the last 150 patients, regarding whom consultations were requested from the university center. Replies were available from 143 cases (95.3%). These replies revealed that neither hospitalization nor sequelae occurred in 68% of the cases, hospitalization but no sequelae in 27%, and sequelae in 5% (at the time of inquiry 2 to 3 weeks after the intoxication); there were no deaths.

The authors believe that poison information centers should help reduce the death rate from intoxication, because they can offer information on most commercial products, including the household agents. However, a listing of ingredients on the container or bottle of all household products would facilitate immediate and specific treatment by physicians of many patients who have been exposed to poisons.

Rabies in Insectivorous Bats of Arizona. W. D. Dean, K. T. Maddy, E. L. Cockrum, and H. G. Crecelius. Arizona Med. 17:69-77 (Feb.) 1960 [Phoenix].

Rabies has been present in Arizona for many years, and the number of laboratory-diagnosed cases has remained fairly constant during the past several years. In 1953 the first case of rabies in a bat ever observed in the United States was diagnosed in Florida. In 1957 the Arizona State Department of Health laboratories diagnosed bat rabies for the first time, and a survey was undertaken to study the epidemiologic significance of rabies in bats in that state. In central and southeastern Arizona during the last half of 1957 and the first half of 1958, 552 bats representing 9 species were collected from 16 sites. All persons collecting bats had received at least 3 intradermal injections of high egg passage chicken-embryo-attenuated (Flury strain) rabies vaccine. The bats were killed with chloroform. The brains were pooled in multiples of 5, and each pooled composite was inoculated into 5 mice. A similar procedure was followed for the salivary glands. Rabies virus was isolated from the following species: big brown bat (Eptesicus fuscus), Mexican free-tail bat (Tadarida brasiliensis mexicana), cave myotis bat (Myotis velifer), and pallid bat (Antrozus pallidus). At least 13 different bats were found to be infected with the rabies virus. Considering the vast geographic area and the millions of bats living in the area, this study was only a superficial sampling. Nevertheless, it gave some indication that rabies in bats is a public health problem in Arizona.

BOOK REVIEWS

Biochemical Aspects of Neurological Disorders. Edited by John N. Cumings, M.D., F.R.C.P., Professor of Chemical Pathology, Institute of Neurology, National Hospital, London, and Michael Kremer, M.D., B.Sc., F.R.C.P. Cloth. $8.75. Pp. 230, with illustrations. Charles C Thomas, Publisher, 301-327 E. Lawrence Ave., Springfield, Ill.; Blackwell Scientific Publications, Ltd. 24-25 Broad St., Oxford, England; Ryerson Press, 299 Queen St., W., Toronto 2B, Canada, 1959.

For the neurologist, biochemistry represents the future, as is amply demonstrated by this short volume of lectures delivered in 1957 and 1958 at the Institute of Neurology, National Hospital, Queen Square, London. These lectures, by 19 British biochemists and neurologists, were designed to bring together the biochemical and clinical aspects of a variety of neurological disorders not readily available in textbooks. The chapters are paired, in effect, each pair presenting in order the chemical and the broad clinical features of the vitamin-B deficiencies, demyelinating diseases, porphyria, disorders of calcium and phosphorus metabolism, copper metabolism, neurological aspects of liver disease, anoxic and hypoglycemic states, pituitary and adrenal dyscrasias, the lipidoses, and disorders of muscular function. A carefully chosen bibliography follows each chapter, and a good index increases the book's reference value.

It will be readily appreciated that a discussion of both chemical and clinical aspects of so vast a field within scarcely more than 200 pages must be but a sketchy survey; indeed, it is as a general survey that this symposium excels. The serious student can do no better than to begin here, but he must proceed at once to the more detailed studies cited and to the more extensive monographs available. Among these, "Neurochemistry," edited by K. A. C. Elliott, I. H. Page, and J. H. Quastel (Charles C Thomas, Publisher, Springfield, Ill., 1955), "Biochemistry and the Central Nervous System," by Henry McIlwain (Little, Brown and Company, Boston, 1955), and, in a related but largely separate field, "Chemical Concepts of Psychosis," edited by Max Rinkel and H. C. B. Denber (McDowell, Oblinsky, New York, 1958) should be mentioned. For the neurologist, the clinical chapters here are elementary and far too sketchy to add greatly to his knowledge; one suspects that the biochemist would view the chemical chapters as similarly elementary. Each, however, should find the other's field admirably presented for his purposes. In particular, clinicians in neurology need the biochemical information so conveniently and briefly gathered here and should find in the book a revelation of the extensive relevancy of biochemistry to their daily work and of the promising future it offers for further advances in diagnosis and therapy.

The authors are among the most eminent in the world; their admirably succinct discussions are judicious and free of quirk and bias, and their guidance is sure to further study. Not only is this small volume to be recommended but it is to be urged on all persons interested in neurological disease.

Roland P. Mackay, M.D.

Isotopic Tracers: A Theoretical and Practical Manual for Biological Students and Research Workers. By G. E. Francis, Reader in Biochemistry, St. Bartholomew's Hospital Medical College, London, W. Mulligan, Senior Lecturer in Biochemistry, Glasgow University Veterinary School, Glasgow, and A. Wormall, Professor of Biochemistry, St. Bartholomew's Hospital Medical College. With foreword by G. Hevesy. Second edition. Cloth. $8.40; 52s. 6d. Pp. 524, with illustrations. Essential Books Division, Oxford University Press, Fair Lawn, N. J.; 417 Fifth Ave., New York 16; Athlone Press, University of London, 2 Gower St., London, W. C. 1, England; distributed by Constable & Company, Ltd., 12 Orange St., London, W. C. 2, England; University of Toronto Press, Toronto 5, Canada, 1959.

This book is written as an introduction to the theoretical principles and practical applications of isotope methodology in the biological sciences. The contents of the text are divided into two parts. In the first part the authors deal with preparation of labelled compounds, measurement of stable and radioactive isotopes, determination of radioisotopes in biological preparations, interpretations of radioactivity measurements, radioautography, hazards and safeguards in the use of radioisotopes, examples of radioisotopes used in biological work, and use of isotopic tracers in the study of the kinetics of biological processes. This part of the text is a carefully selected sampling of the work done in the field. The examples are chosen to give the student a broad background in the application of both stable and radioactive isotopes used in biological studies.

The second part of the book contains a series of practical exercises designed to teach the student the techniques of handling and measuring isotopes in a variety of biological applications. The choice of experiments has been limited to exercises which can be completed in one or two laboratory periods of five or six hours. The equipment specified is of British origin. This, however, should not diminish the value of the book appreciably as the equipment is fairly standard and it should not be difficult to obtain suitable counterparts. This excellent book is based on the material presented in a course in isotopic tracer methodology at the Medical College of St. Bartholomew's Hospital, London. The text should prove of great help to anyone planning to give a similar course, and it should find wide readership among biologists who are daily depending more on tagged molecules to find the answers to their unsolved problems.

JOSEPH ROYAL, Ph.D.

Intussusception in Infants and Children. By Mark M. Ravitch, M.D., Associate Professor of Surgery, Johns Hopkins University School of Medicine, Baltimore. Pediatric surgical monograph series. Edited by Mark M. Ravitch. Cloth. $9. Pp. 121, with illustrations. Charles C Thomas, Publisher, 301-327 E. Lawrence Ave., Springfield, Ill.; Blackwell Scientific Publications, Ltd., 24-25 Broad St., Oxford, England; Ryerson Press, 299 Queen St., W., Toronto 2B, Canada, 1959.

This, the first monograph in a series of pediatric surgical monographs, presents a historical account, the incidence of occurrence, the clinical course, errors in diagnosis, pathological and experimental studies, and the treatment related to intussusception. An excellent diagram demonstrates the various types of intussusception that may be caused by the appendix or originate at the ileocecal junction. The operative treatment of irreducible intussusception is presented as an illustration and includes such procedures as exteriorization of the intestine with delayed division, and resection with primary anastomosis. Nonoperative reduction by barium enema with serial roentgenograms and case histories in the legends is easily followed by the reader. The case fatality figures quoted favor the nonoperative type of reduction. A brief account of the primary treatment with barium enema followed by completion of reduction by operation is given, and illustrative cases are cited.

The author concludes that all children with intussusception deserve a trial with barium enema and feels that between 70 and 75% may be cured by this treatment. He warns against persistence with the barium enema after a point is reached where further progress in reduction ceases. If this occurs, he recommends operation without delay. The format, printing, and illustration in this monograph are excellent for easy readability. The bibliography should be of great value for students of this subject.

ARTHUR F. ABT, M.D.

Medical X-ray Technique: Principles and Applications. By G. J. van der Plaats. Translated by G. E. Luton. Published in English, Spanish, German and French languages. Cloth. $10. Pp. 480, with 229 illustrations. The Macmillan Company, 60 Fifth Ave., New York 11; N. V. Philips' Gloeilampenfabrieken, Kastanjelaan, Eindhoven, Netherlands, 1959.

This textbook is different from the usual one on this subject in that discussions of radiographic positioning, centering, and exposure factors are not included. However, a detailed and thorough discussion of the principles and varied applications of x-ray in diagnosis and therapy, particularly for technicians in training, is presented. The first chapter deals with the discovery of x-ray, definitions, origin of x-ray, and the structure and operations of the x-ray tube. Subsequent chapters cover in adequate detail the entire field of x-ray technique, with emphasis on basic principles. The subject matter is presented in such a manner that the technician will be well versed in all phases, from the nature and properties of x-ray and apparatus to the varied applications in diagnosis as well as therapy. Chapters dealing with image formation and perceptibility, sharpness, contrast, and detail are most informative. A chapter on radioactive isotopes is included in the section on therapy. The genetic and biological effects of radiation are discussed. The final chapter deals with radiation hazards and protective measures in x-ray diagnosis and therapy.

This book has been published in English, Spanish, German, and French. The subject matter is well organized, adequately illustrated, and covers the basic principles and application of x-ray in both diagnosis and therapy. Since it does not include the subjects of positioning, centering, or film exposure factors, it is recommended to the technician as a supplement to other books dealing with these phases of technique. This book should be in the library of every director of a training school for x-ray technicians.

EARL E. BARTH, M.D.

Cancer and Allied Diseases of Infancy and Childhood. Edited by Irving M. Ariel, M.D., Associate Professor of Clinical Surgery, New York Medical College, New York, and George T. Pack, M.D., Associate Professor of Clinical Surgery, Cornell University Medical College, New York. 27 contributing authors. Cloth. $22.50. Pp. 605, with illustrations, Little, Brown & Company, 34 Beacon St., Boston 6; J. & A. Churchill, Ltd., 104 Gloucester Pl., Portman Sq., London, W. 1, England, 1960.

The editors of this volume have correctly interpreted a need for a concise presentation, in one volume, of the problems of cancer and allied conditions in the pediatric age group. They wisely use the experience of others in the compilation of a multiple-author book. Such books often lack continuity, but in the main, the editors have here avoided this. The chapters on intrathoracic tumors and cysts, Wilms's tumors, tumors of the central nervous system, and leukemia and lymphoma are particularly good. One of the difficulties in preparing a book of this kind is to decide whether the chapters should be divided along anatomic or pathological lines, and although the authors generally follow the former classification they deviate from it in the chapter on teratoid tumors and dermoid cysts. One of the fine aspects of the book is its extensive bibliography. Several unusual chapters contribute to the versatility of the book, including the chapters on anemia of cancer in childhood and principles of radiation therapy for tumors in children.

Two criticisms might be leveled against the book. There is the inevitable overlap of treatment in several chapters, and several of the authors have presented a fuller development of their subject than is in keeping with the general outline of the book. This is particularly true of the chapters entitled Pre and Postoperative Care of Infants and Children and Tumors and Hyperplasias of the Adrenal Gland. Almost monographic consideration of these two subjects is undertaken. The value of the book would not have been diminished by a greater condensation of these chapters.

This worthwhile volume should be a valuable aid in the treatment of children with cancer.

William B. Kiesewether, M.D.

Textbook of Otolaryngology. By David D. DeWeese, M.D., Clinical Professor of Otolaryngology, University of Oregon Medical School, Portland, and William H. Saunders, M.D., Associate Professor of Otolaryngology, Ohio State University College of Medicine, Columbus. Cloth. $8.75. Pp. 464, with 354 illustrations. C. V. Mosby Company, 3207 Washington Blvd., St. Louis 3; Henry Kimpton, 134 Great Portland St., London, W. 1, England, 1960.

This first edition is intended primarily for medical students and practitioners but may be read with pleasure and profit by others more advanced in the specialty. It is clear, concise, authoritative, up-to-date, and stylistically unique. Unlike the conventional textbook, it is not encumbered with combinations of the outworn, the new, or the bow to tradition. These authors have opinions and they make them known. There is no need to discuss the various chapters, as they are more than adequate, and the illustrations are excellent. Works reflecting strong personalities, such as this, are rare. It is a distinct pleasure to recommend it.

Samuel J. Pearlman, M.D.

Weight Gains, Serum Protein Levels and Health of Breast Fed and Artificially Fed Infants, Full Term and Premature: A Clinical and Biochemical Study Based on 946 Infants and Children at the Mothers' Hospital (Salvation Army) and the Queen Elizabeth Hospital for Children, London. By B. Levin, M.D., Ph.D., and others. Privy Council, Medical Research Council special report series no. 296. Paper. $2.99. Pp. 154, with illustrations. Her Majesty's Stationery Office, P. O. Box 569, London, S. E. 1, England; American agent: British Information Services, 30 Rockefeller Plaza, New York 20, 1959.

This paper-covered book reports a study to establish standards of serum protein levels in full-term and premature infants, both breast fed and given a dried-milk formula. The variables studied include sex, birth weight, multiple birth, weight gain, hemoglobin values, and electrophoresis of serum proteins. The book is divided into four parts.

Part 1 deals with weight gains and hemoglobin levels of full-term and premature infants, with a comparison of the progress of breast fed and formula fed infants. The protein requirements of premature infants are also included. Part 2 reports on the total serum protein, albumin, globulin, and nonprotein nitrogen levels of full-term and premature infants. The effects of birth weight, age, sex, feeding, and other factors on these levels are given. Part 3 covers the serum protein components as determined by paper electrophoresis and by salt precipitation. There is special reference to gamma globulin. Part 4 summarizes both the clinical and laboratory data.

The material presented is well outlined in tables and figures. There is an adequate bibliography and a comparison with other reported studies on protein requirements. This study was made between 1947 and 1950. It should be of interest to those concerned with infant nutrition.

John A. Bigler, M.D.

A Practice of Anaesthesia. By W. D. Wylie, M.A., M.B., M.R.C.P., and H. C. Churchill-Davidson, M.A., M.D., F.F.A.R.C.S. Cloth. $20. Pp. 1056, with 246 illustrations. Year Book Publishers, Inc., 200 E. Illinois St., Chicago 11; Lloyd-Luke (medical books) Ltd., 49 Newman St., London, W. 1, England, 1960.

This large book contains most of the information a physician might need to pass the examinations of the American Board of Anesthesiology. For the senior anesthesiologist it should be a thrilling revelation to peruse this book and see how the specialty has grown in one lifetime. The relevant aspects of physics, anatomy, and pathology as they relate to the specialty have been touched on; the relevant facets of physiology and pharmacology have been treated in detail; and the clinical applications have been repeatedly emphasized. The book is printed on good paper, is easy to read, and is indexed. Each subject has its own bibliography. Without doubt, this is the best book available on the market today for those who are interested in anesthesiology.

John S. Lundy, M.D.

Roentgenologic Diagnosis in Ophthalmology. By Edward Hartmann, M.D., Chief of Ophthalmic Department, Lariboisière Hospital and American Hospital in Paris, and Evelyn Gilles, M.D., Chief of Roentgenology Department, Quinze-Vingt Ophthalmic Hospital, Paris. Translated by George Z. Carter, M.D., Assistant Professor of Ophthalmology, Albert Eistein College of Medicine, New York. Edited by Conrad Berens, M.D., F.A.C.S., Lecturer in Ophthalmology, New York University Post-Graduate Medical School, New York. [Original French edition appeared under title *Radiodiagnostic en ophthalmologie,* published by Masson & Cie, Paris.] Cloth. $15. Pp. 375, with 497 illustrations. J. B. Lippincott Company, E. Washington Sq., Philadelphia 5; 4865 Western Ave., Montreal, Canada; Pitman Medical Publishing Company, Ltd., 39 Parker St., London, W. C. 2, England, 1959.

In April, 1936, the author published an atlas of clinical radiography in ophthalmology which was soon out of print. Twenty years later, Hartmann, in cooperation with Evelyn Gilles, a roentgenologist, published a new book in French on roentgenologic diagnosis in ophthalmology. It was mainly to serve as a reference for the roentgenologist and ophthalmologist in solving problems encompassing these two specialties. It is this text that has been competently translated. The book is unusually well illustrated with roentgenographic reproductions and line drawings showing the main landmarks. An unusual variety of films of pathological lesions is presented together with pictures of normal anatomic variations. Techniques that are relatively new have been presented in the detection of intraocular foreign bodies. Generally this book is well written, and it will probably become a standard reference for the ophthalmologist and a help to the roentgenologists in considering ophthalmologic problems.

Frank W. Newell, M.D.

Emotional Forces in the Family. Edited by Samuel Liebman, M.D., Medical Director, North Shore Hospital, Winnetka, Ill. Cloth. $5. Pp. 157. J. B. Lippincott Company, E. Washington Sq., Philadelphia 5; 4865 Western Ave., Montreal 6, Canada; Pitman Medical Publishing Company, Ltd., 39 Parker St., London, W. C. 2, England, 1959.

This book is a symposium based on a series of lectures given at the North Shore Hospital in Winnetka, Ill. It is the fifth in a series. The subjects covered by nine physicians, many of whom are psychiatrists, include the development of the family in the technical age; the role of the mother and father and children in the family; the emotional impact of in-laws and relatives; the effect of aging persons on family life; the individual, the family, and the community; the individual, the family, and the boss; and the disintegrating impact of modern life on the family in America and its explosive repercussions. This is a book distinctly for the physician, the psychiatric nurse, and the psychiatric social worker. It is too technical, and too frightening in many aspects, for the nonmedical reader. It should be a valuable handbook for the general practitioner in helping to recognize and interpret the emotional forces that influence the physical symptoms which bring patients to his office.

W. W. Bauer, M.D.

Health Services in the USSR. Report prepared by participants in study tour organized by World Health Organization. *World Health Organization public health papers no. 3.* Paper. 3s. 6d.; 60 cents; 2 Swiss francs. Pp. 58, with illustrations. World Health Organization, Palais des nations, Geneva, Switzerland; Columbia University Press, International Documents Service, 2960 Broadway, New York 27, 1960.

This report presents an outline of the organization, operation, facilities, and programs of health services in the Soviet Union as studied by representatives of 21 countries and involving six areas of the U. S. S. R. Information includes organizational charts and descriptive material on the administrative structure for the ministry of health, rural medical district, city hospital, and factory medical and sanitation department. Material on the incidence and treatment of major diseases, environmental and occupational health, sanatoriums, and medical and paramedical training is presented, but little mention is made of financing, mental health, and geriatrics. The study, sponsored by the World Health Organization, took somewhat more than five weeks to complete, and a large amount of the information was supplied by the U. S. S. R. without the advantage of any comparative study by the group. However, the report should interest both public health officers and medical educators.

Charles Chapman

The Emergency Syndromes in Pediatric Practice. By Alfred J. Vignec, M.D., *Clinical Professor of Pediatrics, New York University, College of Medicine, New York.* Cloth. $9. Pp. 382, with 14 illustrations. Landsberger Medical Books, Inc., 51 E. 42nd St., New York, 1959.

This well-written, informative book includes 10 chapters, with a good short outline of the material included in each chapter. The material is well presented, easy to read, and covers the most important emergency syndromes seen in pediatric practice. The index is not as complete as it should be; one has difficulty in locating specific references in the text. For instance, under acidosis one finds only a reference to burns and under dehydration, only hyponatremia and pyloric stenosis. No mention is made of hypernatremia, which has become an important problem in pediatric emergencies.

The material on fluid and electrolyte replacement is good, but, as in other texts, there is no explanation as to how it is determined that 1.8 cc. of sixth molar lactate raises the carbon dioxide level one volume per 100 ml. and 1.5 cc. of sixth molar ammonium chloride lowers the carbon dioxide level one volume per 100 ml. This is a worthwhile textbook on pediatric emergencies as seen by the general practitioner and the pediatrician.

John A. Bigler, M.D.

The Megaloblastic Anemias. By Victor Herbert, M.D., Research Assistant in Hematology, Mount Sinai Hospital, New York. Modern Medical Monographs 18. Editor-in-chief: Irving S. Wright, M.D. Consulting editor: Richard H. Orr, M.D. Cloth. $6. Pp. 162, with illustrations. Grune & Stratton, Inc., 381 Fourth Ave., New York 16; 15/16 Queen St., Mayfair, London, W.1, England, 1959.

The inclusion in this volume of over 600 references indicates the thoroughness with which Dr. Herbert has reviewed the literature on the megaloblastic anemias. A student of these disorders, the author has digested and evaluated the great variety of studies that have been made in this field and has crystallized this information effectively. This is useful and thoughtful monograph.

M. M. Wintrobe

QUESTIONS AND ANSWERS

UNDESCENDED TESTES AND GYNECOMASTIA

To the Editor:—*A 31-year-old man has had progressive enlargement of his breasts for four to five months. He also has undescended testes which have responded neither to hormonal therapy nor to two operative attempts to bring them down from the inguinal canals and only one of which is palpable. He has a normal male body contour, gynecomastia, sparse axillary and pubic hair, a normal penis, and an atrophic scrotum. The prostate gland is not palpable. He is potent but sterile. Is his gynecomastia due to atrophy of the undescended testes? What therapy should be given for the breast enlargement? Should the testes be removed?*

M.D., Massachusetts.

Answer.—Gynecomastia is rarely encountered in patients with undescended testes. Other conditions associated with gynecomastia should be considered, especially in this patient, because of the recent development of the gynecomastia. It is possible that the gynecomastia is related to testicular atrophy due to gonadal dysgenesis or to mechanical trauma from attempted repair of cryptorchism. Determination of the sex chromatin pattern may be helpful in the diagnosis of gonadal dysgenesis. Feminizing tumors of the testis or adrenal glands should be considered; measurement of urinary estrogen excretion would be helpful in this regard. Embryonal cell carcinoma or chorionepithelioma of the testis may be associated with gynecomastia. Measurement of urinary chorionic gonadotropin levels would be helpful in this diagnosis. Cirrhosis of the liver or hepatitis may be associated with gynecomastia, perhaps because of failure to eliminate estrogens. Gynecomastia may be due to the administration of hormones, such as chorionic gonadotropin, estrogens, or androgens. The gynecomastia usually subsides on withdrawal of the hormones. Digitalis can produce gynecomastia.

Hormone therapy is usually unsuccessful in the treatment of gynecomastia. Gynecomastia may subside after removal of a hormone-producing tumor. If necessary for psychic reasons, surgical removal of the breast tissue is the treatment of choice. Removal of the testis which cannot be palpated is probably indicated in this patient. Gynecomastia may be the earliest manifestation of testicular tumor. If tumor is not present, pathological examination may give differential diagnostic information between gonadal dysgenesis and simple cryptorchism.

CALCIFICATION OF INTERNAL CAROTID ARTERY

To the Editor:—*This question is a result of the current interest in carotid artery insufficiency as an etiological factor in unilateral cerebral disease. What is the significance of calcification in the walls of the internal carotid artery where it arches above the sella turcica, as seen in lateral roentgenograms of the skull? Have any studies been carried out to determine the incidence of such roentgenographic evidence of calcification of the internal carotid artery in this area in each age and sex group? Can one conclude that such calcification in a man aged 20 years is pathological?*

Joseph Amdur, M.D., Long Beach, L. I., N. Y.

Answer.—Nerli found carotid siphon calcification in 32.9% of 1,483 roentgenograms of the skull; calcification was severe in 3.5%. More common in male patients, the incidence increased with age. It was found in only three patients under 30 years of age. In a series of 36 roentgenograms of the basisphenoid region with the carotid arteries, after removal at autopsy, 28 showed calcification which, the author concluded (probably erroneously), corresponded to atherosclerosis on gross examination.

Fisher, in a small series of autopsy specimens of the carotid siphon, showed calcification in 100% on roentgenograms taken after removal from the skull. Histologically this calcium could lie in three sites: in the elastic lamina, in the media, or in an intimal atherosclerotic plaque. The most common location was the elastic lamina and adjacent inner media, which corresponds to the linear calcification so frequently seen in routine roentgenograms of the skull. This form of calcification was not directly related to the presence of atherosclerosis either locally, in the cerebral arterial tree, or in the aorta; it could be minimal in the presence of severe atherosclerosis or, conversely, severe with little or no atherosclerosis. In most cases a moderate amount of each was present. The linear calcification occurred first in the internal elastica, tending to "spare" the region underlying a plaque of atherosclerosis. Hypertension appeared to aggravate it. The calcification in atherosclerotic plaques was an entirely different process, showing in postmortem roentgenograms as opaque plaques; these are rarely visible in routine skull films.

The answers here published have been prepared by competent authorities. They do not, however, represent the opinions of any medical or other organization unless specifically so stated in the reply. Anonymous communications cannot be answered. Every letter must contain the writer's name and address, but these will be omitted on request.

It is difficult to evaluate calcification in a 20-year-old man. Other causes of parasellar calcification must be ruled out. If it is arterial and linear, it probably bears no relation to atherosclerosis. A congenital fusiform or tubular aneurysm of the carotid siphon may show premature calcification. Hypercalcemia, a vegetarian diet, hypervitaminosis, hypertension, or cerebral angioma may be implicated.

References

Nerli, A.: Le calcificazioni delle carotidi interne intracavernose: Semeiotica radiologica, Radiol. med. **41:**676-686 (July) 1955.

Fisher, C. M.: Unpublished data.

ALLERGENIC SUBSTANCES FROM INSECTS

To the Editor:—*What is butterfly fever and where is it found?* *M.D., Illinois.*

Answer.—A search through the available literature has failed to reveal the term "butterfly fever" documented as such.

If the term butterfly fever is an indigenous one, developed through local usage, and relates to an allergic condition, the following information is pertinent.

Insects may be a source of inhalant allergens and the cause of sensitivity. Insects of the Lepidoptera order, which includes various species of moths, butterflies, and caterpillars, have been incriminated. Caffrey, an entomologist, working with the New Mexico range moth, described in himself and several co-workers hay fever-like symptoms, including violent paroxysms of coughing and sneezing, which he attributed to contact with moth hairs. Butterfly scales are an exogenous allergen, and the caddis fly, a sand fly, prevalent in the Great Lakes region, can also cause an inhalant allergy. One source of reference states, "Parlato has demonstrated allergy to the emanations of moths and butterflies. The caddis fly is closely related to the moth, resembling the common clothes moth in size and shape. Caddis flies, moths and butterflies are the only insects which shed hairy scales. Parlato presents evidence of crossed sensitization and believes that a person allergic to any of these three will react to an extract of any one. The hairs and scales of moths and butterflies are often seen on pollen slides and may actually far outnumber the pollens. According to Balyeat, Stemen, and Tafk the scales appear on slides in June and July in Oklahoma at about the time of the grass season and are far more numerous than the grass pollen grains."

Perlman speculated on the role that component substances of insect cuticle, such as chitin and arthropodin, play in the production of insect allergy. He concluded, however, that these roles are not clearly defined. Silk, which is produced by many insects, also is reported to be an allergen.

Insect allergens have been prepared for use in treatment of these conditions, but conclusive results have not yet been reported.

References

Perlman, F.: Insects as Inhalant Allergens, J. Allergy **29:** 302 (July) 1958.

Wiseman, R. D., and others: Insect Allergy as a Possible Cause of Inhalant Sensitivity, J. Allergy **30:**191 (May-June) 1959.

COCCYGODYNIA

To the Editor:—*Please describe the treatment of coccygodynia, including conservative methods. Is injection of hydrocortisone indicated?*

R. S. Srigley, M.D., Altus, Okla.

Answer.—The treatment will vary, depending on whether the condition is of recent origin or chronic. When treating a patient with acute coccygeal pain, one must determine whether it is due to disk protrusion, which may be accompanied by coccygeal pain, or to a primary injury to the coccyx.

The usual symptoms and signs of acute injury to the coccyx are pain with sitting, stooping, and defecation and local tenderness on palpation. Roentgenographic examination must always be made to determine the presence of a fracture, dislocation, asymmetry, or osteoarthritic change. The treatment is primarily rest of the injured part. Manual reduction of a dislocation or a displaced fracture should be attempted and may have to be repeated several times. The patient should be instructed by the physician how to keep his body weight off the coccyx; this involves proper sitting posture, usually on a firm chair, and use of a rubber ring or sponge cushion. Procaine hydrochloride and hydrocortisone may be injected locally. Some physicians feel that adhesive strapping or use of a sacroiliac belt is helpful. Physical therapy, such as locally applied heat, massage, and use of ultrasonic waves may also be valuable adjuncts in the treatment of a patient with an acute case. The patient with acute coccygodynia should be warned, at the outset, that his recovery may take several weeks or possibly a few months.

In a chronic case, roentgenograms should be made to rule out the possibility of a local tumor, osteomyelitis, tuberculosis, and various other local diseases which occasionally cause coccygodynia. A lumbar disk protrusion should be ruled out. The physician should be sure he is not dealing with a patient who has a psychoneurotic personality.

The treatment of the patient with a chronic case of coccygodynia encompasses the trial of many modalities mentioned above in the treatment of an acute case. Procaine hydrochloride and hydrocortisone injections should certainly be administered and should be repeated if necessary. If these measures fail, and if the patient is not of a basically psychoneurotic personality type, coccygectomy should be offered. The published results in selected cases of coccygectomy have been satisfactory in from 75 to 90% of patients.

REPOSITORY ALLERGY INJECTIONS

To the Editor:—*Is a one-shot desensitization treatment for hay fever, involving single annual injections of emulsified extract, a medically acceptable procedure, or is it still in the experimental stage? They are referred to as "repository allergy injections." If this procedure is still a matter of controversy, please advise where I may obtain some up-to-date medical literature and opinions regarding its use.*

Lyle G. Ellis, M.D., Hartford, Conn.

Answer.—Repository pollen injections were first advocated by Loveless (*J. Immunol.* 79:68 [July] 1957) and, in the last couple of years, have been publicized through the enthusiastic reports of Brown (*Ann. Allergy* 17:358 [May-June] 1959). There are several phases of such treatment that must be investigated by a larger group of critical observers and for a longer period before such therapy can be recommended for general use. The questions that must be determined are as follows: the effectiveness of such treatment, particularly in areas of high ragweed incidence; establishment of conditions that will prevent constitutional reactions; and the possibility of producing new types of hypersensitivity and other reactions from long-term treatments. An attempt is being made to study these and other factors under controlled conditions by a selected group of allergists under the supervision of a special committee of the Research Council of the American Academy of Allergy. Anyone interested in such therapy should definitely await the outcome of these studies. Reports by Criep and associates and Feinberg and associates are due for publication in the *Journal of Allergy.*

DIAGNOSTIC VALUE OF ELECTROENCEPHALOGRAMS

To the Editor:—*Please clarify the following problem in semantics, which has medicolegal implications. When an electroencephalographic report reads "compatible (or consistent) with alcoholism, immaturity, behavior disorder, or mental deficiency," are the words "compatible with" or "consistent with" tantamount to a diagnosis of such conditions or states?* *M.D., California.*

Answer.—The words "compatible with" or "consistent with," when used in the interpretation of a laboratory test such as an electroencephalogram, usually constitute a protective device that has been developed so that persons who are properly trained to read the tracings but do not hold a medical degree can remain within the law by not making a diagnosis. Such terminology is rarely used by neurologists and physicians, who interpret the electroencephalogram and integrate the findings with the clinical problem. Occasionally, medically trained interpreters who have had inadequate experience and training in electroencephalography use this device. The equivalent to this expression, freely translated, would be "this particular record may or may not fit this particular diagnosis."

On the other hand, there are few situations in which the electroencephalographic picture alone can lead to a clinical diagnosis. One situation in which this is possible is when a patient, while the recording is being made, has a brief clinical seizure accompanied by a characteristic seizure pattern, such as the spike-and-wave discharge, on the tracing. If the technician notes that a brief interval of unresponsiveness occurred during the period of the spike-and-wave discharge, the integration of this observation with the electroencephalographic findings establishes a diagnosis of a brief "absence" or petit mal seizure or a specific form of epilepsy. The electroencephalographic record alone, however, without the clinical finding, would not establish a diagnosis of epilepsy. A clinical diagnosis cannot be made from the findings of a laboratory test such as this without the integration of clinically observed data and a clinically factual history. This must be done by a licensed and properly trained physician. A number of textbooks, such as Harrison's "Principles of Medicine," contain discussions of this problem.

UNSUCCESSFUL ATTEMPTS AT SMALLPOX VACCINATION

To the Editor:—*What method of smallpox vaccination should be used in a 5-year-old boy in whom five separate attempts have failed to produce a primary reaction? He had not been vaccinated prior to these attempts, in which the scratch and multiple pressure techniques were used.* *Melvin I. Roth, M.D., Gary, Ind.*

Answer.—When repeated failures in primary vaccination have occurred, a fresh lot of vaccine should be used. Potency and activity may be assured by demonstrating the capacity of vaccine from this lot to produce a primary reaction in other children. To preserve potency, vaccine should be kept frozen except when used. Vaccination may be tried at another site, such as the opposite arm away from the area of previous attempts. The outer surface of the arm is the best location. The skin should be thoroughly cleaned with acetone and allowed to dry. The multiple pressure technique is preferable. Absence of reaction is not evidence of immunity; it indicates an unsuccessful effort. Vaccination should be repeated until a primary reaction is obtained.

ABNORMAL GROWTH OF AN INFANT

TO THE EDITOR:—*A 28-month-old girl has an infantile body, a somewhat large head, and an elfin facial appearance. There is a congenital ptosis of the left lid. Physical findings are otherwise not remarkable. The family history reveals that many members of both families have been of short stature, with an average height of 5.5 ft. The infant has been well since birth, except for some early feeding difficulties and repeated upper respiratory infections. The latter have been reduced by continued administration of gamma globulin. About one year ago her serum gamma-globulin levels were discovered to be in the range of 5 to 6 Gm.% or about what we consider one-half normal. Normal laboratory findings were obtained for urinalysis, blood count, carbon dioxide-combining power, and levels of calcium, chloride, nonprotein nitrogen, phosphorus, alkaline phosphatase, potassium, sodium, and cholesterol. The protein-bound iodine level was 6.2 mcg.%. The glucose tolerance test (oral) showed a fasting level of 79 mg. per 100 cc.; the highest level was 90 mg. per 100 cc., and it returned to 77 mg. in six hours. The value of urinary pituitary gonadotropins was 75 mouse units (M. U.). Her bone age was roentgenographically determined to be about one year. Considering the elevation in urinary pituitary gonadotropins, is one justified, at this time, in making a diagnosis of ovarian agenesis? If so, what treatment should be given?*

P. L. Wachtel, M.D., Freeport, Ill.

ANSWER.—A diagnosis of ovarian agenesis or gonadal dysgenesis is justified if the child persistently excretes measurable amounts of pituitary gonadotropins in her urine. No treatment is indicated until she reaches the age of adolescence, when estrogen therapy may induce the development of secondary sex characteristics.

While gonadal dysgenesis is frequently associated with such congenital abnormalities as webbing of the neck, cubitus valgus, low placement of the hairline, and hypertension, elfin facial features, low-placed ears, and deficiency of gamma globulin are not considered part of the syndrome. A satisfactory growth-promoting substance is not available for general clinical use.

TREATMENT FOR SARCOIDOSIS

TO THE EDITOR:—*I have a patient who has Boeck's sarcoid. What therapy, if any, aside from administration of cortisone acetate, is effective against this disease? At what stage in the course of the disease is it best to initiate therapy?*

Robert F. Zuch, M.D., Chatham, N. J.

ANSWER.—Although much has been accomplished in the last few years regarding the study of sarcoidosis, the true nature of this disease complex has yet to be determined. Specific treatment is usually unnecessary, since spontaneous regression may be anticipated in most patients with this disease. The patient should be reassured about the usually benign course of the disease. Many of the medicaments used in the past have proved ineffective and may cause harm by virtue of their side-effects. A basic program of rest, good nutrition, and observation is usually all that is required.

In selected patients adrenal steroid hormones have been of benefit when used judiciously. In general, they are indicated for the treatment of severe manifestations of the disease which may lead to late permanent sequelae, e. g., in patients with progressive symptomatic pulmonary involvement, or for symptomatic relief from disabling dyspnea resulting from pulmonary fibrosis. Other indications for steroid therapy are the presence of uveitis, persistent hypercalcemia with renal impairment, and direct involvement of the heart and central nervous system. Local application of steroids should be tried on disfiguring skin lesions before systemic therapy is resorted to. The dosage and duration of therapy depend on the duration and severity of the disease and the patient's initial response. In general, doses in the range of 20 mg. daily of prednisone or its equivalent in other steroid forms may be tried. Courses of therapy usually last two to six months but vary with the individual patient. The risk of precipitating or developing active tuberculosis while the patient is receiving steroids is present but in actual practice is not a frequent occurrence. Antituberculous drugs need not be given except to the exceptional patient in whom tuberculosis cannot be definitely excluded.

ROENTGENOGRAPHIC PELVIMETRY

TO THE EDITOR:—*The Colcher-Sussman technique of roentgenographic pelvimetry is now available to me, but I am having difficulty visualizing the symphysis well enough to obtain a good measurement of the true conjugate. Is there a simple method (requiring little extra equipment) which would allow determination of this measurement more accurately?*

Benjamin E. Morgan, M.D.
Rocky Mount, N. C.

ANSWER.—The Colcher-Sussman technique, in which a pelvimeter or some modification of it is used, is probably the commonest method of pelvimetry in the United States. Radiation hazard to fetus and mother is a prime consideration. Exposure should be kept at a minimum; hence repeated exposures should be avoided.

In positioning the patient for lateral projection films, the legs should be extended to avoid overshadowing of the femurs on the symphysis. There must be no rotation of the patient. The responder exposes this lateral projection film with the patient standing rather than recumbent. The true conjugate can also be obtained with use of Albert's position, the patient reclining at an angle of about 55 degrees, so that the pelvic inlet is parallel to the table top and the pelvimeter at the level of the symphysis. In lateral projection the graduated metal ruler is placed between the buttocks, care being taken not to tilt it from the vertical plane. The measurements obtained are, of course, bone measurements; allowance must be made for soft tissue.

PROGESTERONE TEST FOR PREGNANCY

To THE EDITOR:—*Would you comment on the use of orally administered progesterone as a test for pregnancy?*

Frank Howard Richardson, M.D., Asheville, N.C.

ANSWER.—The oral administration of progesterone has proved to be a fairly accurate test for pregnancy but is not as specific as the commonly used biological tests. The test consists of the administration of 200 to 400 mg. of anhydrohydroxyprogesterone daily for three days. If the patient is not pregnant, bleeding will occur three to seven days later. While the failure to bleed at the end of seven days ordinarily indicates pregnancy, other conditions, such as premenopausal amenorrhea, persistent corpus luteum, or corpus luteum cyst, may give a similar negative response. Furthermore, it is possible that the bleeding which is induced (presumably by the hormone administration) may actually be an early symptom of a disturbed pregnancy, i. e., threatened abortion or ectopic pregnancy. The only advantage this method has over the biological tests is that it does not require laboratory facilities to confirm the diagnosis of pregnancy. Other disadvantages in addition to those mentioned above are that 7 to 10 days are required to obtain a result and the possibility that, in spite of the physician's assurance that this medicament cannot produce abortion, the patient may be left with the impression that an early abortion was induced. This test is of practical value only when the ordinary laboratory tests for pregnancy are not readily available.

PROPER USE OF TESTING TAPE

To THE EDITOR:—*I have recently read an article in a popular magazine regarding the use of "Tes-Tape" to determine a woman's ovulatory cycle. The article stated that use of the tape should be discontinued, since it contains chemicals that can cause serious damage to the reproductive organs. I would appreciate comment on this.*

John A. Voss, M.D., Grand Rapids, Mich.

ANSWER.—The tape is impregnated with orthotolidine. This agent is usually used for the detection of sugar in the urine and is generally available without prescription. In view of the chemical relationship of orthotolidine to other agents with known potential for causing abnormal cellular effects, the safety of this novel use of orthotolidine when applied to cervical tissue is not established. The contact between the cervix and this chemical is a new use of this agent and should be considered investigational. The test should be performed under the supervision of a physician who can evaluate the possible adverse effect, if any, on the cervical tissue. Since this new method of testing for ovulation and determining the ovulatory cycle subsequently was described in the lay literature, and since the material was freely available, a note of warning to the public against unsupervised use was issued by the Food and Drug Administration. Investigational studies will eventually show whether and in what manner this drug may be safely used for this new purpose. The full text of the warning statement is available from the U. S. Food and Drug Administration, Washington 25, D. C.

ORIGIN OF THE TERM CHICKENPOX

To THE EDITOR:—*What is the origin of the name chickenpox? I am familiar with the origins of the terms greatpox and smallpox but cannot derive that of chickenpox.*

John E. Beck, M.D., Chamblee, Ga.

ANSWER.—"The name is said to have had its origin in the Latin word 'cicer,' meaning chick-pea. It was so called from the indistinct resemblance of the eruption to chick-peas. Morton was the first to use the term 'chickenpox' and stated that this was its popular name in England." This answer is a quotation from Wain's The Story Behind the Word: Some Interesting Origins of Medical Terms, Springfield, Ill., Charles C Thomas, Publisher, 1958, p. 66.

TRANSFUSION WITH INCOMPATIBLE BLOOD

To THE EDITOR:—*In* THE JOURNAL, *Jan. 2, page 119, there was a question regarding the largest amount of incompatible blood ever given a patient who then survived the resulting reaction. While serving as a resident in anesthesiology in 1950, I observed a case in which three units (1,500 cc.) of blood of the wrong type was inadvertently administered to a woman during performance of a lumbar laminectomy. She had a severe reaction but made a complete recovery. In a search of the literature at that time I could find no instance in which a larger amount of mismatched blood had been given with subsequent recovery of the patient.*

C. F. Crossley Jr., M.D.
908 Sir Francis Drake Blvd.
Kentfield, Calif.

WASHINGTON NEWS

A. M. A. Stand on Administration Plan . .
Private Health Insurance Rise . .
Radiation Dangers Reviewed . .
Federal Research Grants . .
Court Takes Contraceptive Case . .

A. M. A. STAND ON ADMINISTRATION PLAN

The American Medical Association opposed the administration's aged health care program on grounds that it was based "on the false premise that almost all persons over 65 need health care and cannot afford it."

Dr. Louis M. Orr, A. M. A. President, asserted "this is not a fact. The truth is that a *majority* of our older people are capable of continuing a happy, healthy, and, in many cases productive life. Of the more than 15 million persons in the nation over 65 years of age, only 15% are on old age assistance."

The administration plan, offered as a substitute to the controversial Forand bill that would use the social security mechanism to finance health care for the elderly, was designed to aid the aged with limited incomes to buy broad medical and hospital insurance. Under the voluntary plan, the elderly who were able to do so would pay part of the cost of both medical and hospital care as well as of the insurance. Estimated cost of the federal and state governments was 1.2 billion dollars annually. Only those aged with less than specified incomes could participate.

Dr. Orr said neither the administration's proposal nor the Forand-type social security approach is geared to meet the problems of older persons who, "although able to finance other costs, find it difficult to withstand the additional burden of the cost of illness."

He proposed the A. M. A.'s positive eight-point program for the health care of the aged as a "sensible, economical" plan that would preserve freedom as well as promote security. If both these objectives are to be realized, Dr. Orr said, health care programs for the aged "must necessarily be limited to support for the needy aged and leave to voluntary, competitive, private enterprise, those activities needed to improve the health care of the rest."

In summary, the A. M. A. program calls for (1) improved preventive medical care for the aged; (2) a state-administered program of federal grants-in-aid to states for liberalization of existing old-age assistance programs so that the near-needy could be given health care without having to meet the present rigid requirements for indigency; (3) better nursing-home facilities for the long-term care of aged persons, especially those over 75 years of age; (4) rapid development of health insurance and prepayment policies to provide long-term nursing home care; (5) expansion of home nursing care services; (6) elimination of compulsory retirement and a basic change in the attitude that a person who reaches 65 has suddenly become nonproductive and senescent; (7) health education to instill a "will to live" in older persons and to make them aware of the need for continuing healthful nutrition; and (8) anti-inflationary curbs to maintain the purchasing power of fixed pension and annuity benefits.

Later, Dr. Orr, in an address to the Medical Society of the State of New York, said that if Congress passes a medical aid bill for the elderly the nation's hospitals will be jammed with persons who do not need medical care.

"Much of the nation now suffers from lack of sufficient hospital facilities to care for the critically ill of all ages," said the A. M. A. President. "Sending millions of elders with minor ailments to hospitals will turn a serious situation into a chaotic one across the nation," he declared.

The state society earlier had passed a resolution urging Congress to take no action on health care bills until the problem had been studied thoroughly.

AGED HEALTH INSURANCE GAINS

Almost 50% of Americans 65 years of age or older had health insurance at the start of this year, according to the latest survey of aged health insurance coverage.

The survey, conducted by the Health Insurance Association of America, disclosed that of the 15,700,000 persons in this age group, an estimated 7,700,000 had private health insurance.

The growth of health insurance protection among persons aged 65 years and older has been more rapid during the past eight years than for the population as a whole, due to stepped-up activity by insuring organizations, said the Association.

In early 1952, only one of four elderly persons had health insurance, while one out of two are now protected, the survey showed.

In addition to the 49% of the 65-and-over group with health insurance, another 15%—or 2,400,000 persons—are officially classified as indigent, and provision is made for their medical needs through federal-state old age assistance plans.

The association, composed of 270 insurance companies, said one new insuring technique has been the mass enrollment approach of issuing health

(Continued on next page)

MEETINGS

AMERICAN MEDICAL ASSOCIATION: Dr. F. J. L. Blasingame, 535 North Dearborn St., Chicago 10, Executive Vice-President.
1960 Annual Meeting, Miami Beach, Fla., June 13-17.
1960 Clinical Meeting, Washington, D. C., Nov. 28-Dec. 1.
1961 Annual Meeting, New York City, June 26-30.
1961 Clinical Meeting, Denver, Nov. 27-30.
1962 Annual Meeting, Chicago, June 11-15.
1962 Clinical Meeting, Los Angeles, Nov. 26-29.

AMERICAN

1960

June

American Academy of Tuberculosis Physicians, Miami Beach, Fla., June 11. Dr. George P. Bailey, P. O. Box 7011, Denver 6, Secretary.

American Association of Neuropathologists, Statler-Hilton Hotel, Boston, June 11-12. Dr. Leon Roizin, 722 W. 168th St., New York 32, Secretary-Treasurer.

American College of Angiology, Roney Plaza Hotel, Miami Beach, Fla., June 10-12. Alfred Halpern, Ph.D., 11 Hampton Court, Great Neck, N. Y., Executive Secretary.

American College of Chest Physicians, Miami Beach, Fla., June 8-12. Mr. Murray Kornfeld, 112 E. Chestnut St., Chicago 11, Executive Director.

American Diabetes Association, Inc., Hotel Deauville, Miami Beach, Fla., June 11-12. Mr. J. Richard Connelly, 1 E. 45th St., New York 17, Executive Director.

American Electroencephalographic Society, Belmont Hotel, Cape Cod, Mass., June 10-12. Dr. George A. Ulett, 1420 Grattan St., St. Louis 4, Secretary.

American Medical Women's Association, Hotel Carillon, Miami Beach, Fla., June 9-12. Mrs. Lillian T. Majally, 1790 Broadway, New York 19, Executive Secretary.

American Neurological Association, Hotel Statler, Boston, June 13-15. Dr. Melvin D. Yahr, 710 W. 168th St., New York 32, Secretary.

American Physical Therapy Association, Penn-Sheraton Hotel, Pittsburgh, June 26-July 2. Miss Lucy Blair, 1790 Broadway, New York 19, Acting Executive Director.

American Society of X-Ray Technicians, Netherland Hilton Hotel, Cincinnati, June 11-16. Genevieve J. Eilert, R.T., 16 Fourteenth St., Fond du Lac, Wis., Executive Secretary.

American Therapeutic Society, Barcelona Hotel, Miami Beach, Fla., June 9-12. Dr. Oscar B. Hunter Jr., 915 19th St., N. W., Washington 6, D. C., Secretary.

Association for Research in Ophthalmology, Inc., Miami, Fla., June 12-17. Dr. Lorand V. Johnson, 10515 Carnegie Ave., Cleveland 6, Secretary-Treasurer.

Idaho State Medical Association, Sun Valley, June 15-18. Mr. Armand L. Bird, Sonna Bldg., Boise, Idaho, Executive Secretary.

Maine Medical Association, Hotel Samoset, Rockland, June 19-21. Dr. Daniel F. Hanley, P. O. Box 240, Brunswick, Maine, Executive Director.

Northwest Proctologic Society, Roche Harbor, San Juan Island, Wash., June 21-24. Dr. L. D. Leslie, 1162 Willamette St., Eugene, Ore., Secretary-Treasurer.

Society of Biological Psychiatry, Deauville Hotel, Miami Beach, Fla., June 11-12. Dr. George N. Thompson, 2010 Wilshire Blvd., Los Angeles 57, Executive Secretary.

Society for Investigative Dermatology, Inc., di Lido Hotel, Miami Beach, Fla., June 13-15. Dr. Herman Beerman, 255 S. 17th St., Philadelphia 3, Secretary-Treasurer.

Society of Nuclear Medicine, Estes Park, Colo., June 22-25. Dr. Thad P. Sears, Veterans Administration Hospital, Denver 20, Chairman.

Society for Vascular Surgery, di Lido Hotel, Miami Beach, Fla., June 12. Dr. George H. Yeager, 314 Medical Arts Bldg., Baltimore 1, Secretary.

July

American Goiter Association, Church House, London, England, July 5-8. Dr. John C. McClintock, 702 Madison Ave., Albany 8, N. Y., Secretary.

American Society of Facial Plastic Surgery, Hotel Elysee, New York City, July 22. Dr. Samuel M. Bloom, 123 E. 83d St., New York 28, Secretary.

Flying Physicians Association Hawaii Cruise, leaving Los Angeles and San Francisco, July 11. For information write Mr. Mark E. DeGroff, P. O. Box 3275, Tulsa, Okla.

Oregon Cancer Conference (Second Annual), Sheraton Hotel, Portland, July 7-8. Dr. Martin A. Howard, 115 S. W. Taylor St., Portland 5, Ore., Chairman.

Rocky Mountain Cancer Conference, Hilton Hotel, Denver, July 20-21. Mr. Harvey T. Sethman, 835 Republic Bldg., Denver 2, Executive Secretary, Colorado State Medical Society.

August

American Association of Blood Banks, Jack Tar Hotel, San Francisco, Aug. 21-26. For information write: AABB Central Office, Suite 1619, 30 N. Michigan, Chicago 2.

American Congress of Physical Medicine and Rehabilitation, Mayflower Hotel, Washington, D. C., Aug. 21-26. Mrs. [illegible] 30 N. Michigan Ave, Chicago 2, Executive Secretary.

American Hospital Association, Civic Auditorium, San Francisco, A 27-Sept. 1. Mr. Maurice J. Norby, 18 E. Division St., Chicago, Ass Director.

American Institute of Ultrasonics in Medicine, Statler-Hilton H Washington, D. C., Aug. 20. Dr. Dorothy M. Stillwell, Dept. of Med. and Rehab., Univ. of Colorado Med. Center, Denver 20, Cha

American Physiological Society, Stanford University, Calif., Aug. 26. Mr. Ray G. Daggs, 9650 Wisconsin Ave., Washington 14, D. Executive Secretary.

American Society of Clinical Hypnosis, Miami, Fla., Aug. 7-10. Seymour Hershman, 6770 N. Lincoln Ave., Chicago 46, Secretary.

American Society for Pharmacology and Experimental Thera tics, University of Washington, Seattle, Aug. 21-25. Dr. Karl H. Be Merck Sharp & Dohme Research Laboratories, West Point, Pa., Secret

American Veterinary Medical Association, Denver-Hilton Hotel, ver, Aug. 15-18. H. E. Kingman Jr., 600 S. Michigan Avenue, Chi 5, Executive Secretary.

Biological Photographic Association, Inc., Utah Motor Lodge, Lake City, Utah, Aug. 23-26. Miss Jane H. Waters, Box 1668, Gr Central P. O., New York 17, Executive Secretary.

Conference on the Chemical Organization of Cells: Normal Abnormal, University of Wisconsin, Madison, Aug. 25-27. Dr. J. F. McManus, Dept. of Pathology, University of Alabama Medical C Birmingham, Chairman.

Gerontological Society, Inc., Mark Hopkins Hotel, San Francisco, A 7-12. Mrs. Marjorie Adler, 660 S. Kingshighway Blvd., St. Louis 1 Administrative Secretary.

National Medical Association, Inc., Penn-Sheraton Hotel, Pittsb Aug. 8-11. Dr. John T. Givens, 1108 Church St., Norfolk, Va., Ex tive Secretary.

Reno Surgical Society, Mapes Hotel, Reno, Nev, Aug. 18-20. Dr. G bert G. Lenz, 505 S. Arlington Ave., Reno, Nevada.

Rocky Mountain Radiological Society, Denver-Hilton Hotel, Denve Aug. 11-13. Dr. John H. Freed, 4200 E. 9th Ave., Denver 20, Secret Treasurer.

St. Joseph's Hospital Annual Clinics, St. Joseph's Hospital, Den Aug. 3-5. Dr. W. H. Leitch, St. Joseph's Hospital, 1818 Humboldt S Denver 18, Chairman.

West Virginia State Medical Association, The Greenbrier, W Sulphur Springs, Aug. 25-27. Mr. Charles Lively, Box 1031, Charle 24, W. Va., Executive Secretary.

September

American Academy of Pediatrics, and American Academy of Ge eral Practice, Louisiana Chapter, Roosevelt Hotel, New Orlea Sept. 23. Dr. Herbert B. Rothschild, 1520 Louisiana Ave., New Orle 15, Chairman of Publicity Committee.

American Medical Writers' Association, Hotel Morrison, Chicago, Sept. 30-Oct. 1. Dr. Harold Swanberg, 510 Maine St., Quincy, Ill., Secretary.

American Roentgen Ray Society, Ambassador Hotel, Atlantic City, Sept. 27-30. Mr. Hugh Jones, 20 N. Wacker Dr., Chicago 6, Director, Public Relations.

American Society of Clinical Pathologists, Palmer House, Chicago, Sept. 24-Oct. 2. Mr. Claude E. Wells, 445 Lake Shore Drive, Chicago 11, Executive Secretary.

College of American Pathologists, Palmer House, Chicago, Sept. 24-27. Dr. Arthur H. Dearing, 2115 Prudential Plaza, Chicago, Executive Director.

Colorado State Medical Society, Stanley Hotel, Estes Park, Sept. 14-17. Mr. Harvey T. Sethman, 835 Republic Bldg., Denver 2, Executive Secretary.

Delaware, Medical Society of, Rehoboth, Del., Sept. Mr. Lawrence C. Morris Jr., 1925 Lovering Ave., Wilmington 6, Del., Executive Secretary.

Flying Physicians Association, third clinical meeting, Western Hills Lodge, Wagoner, Okla., Sept. 6-9. For information write: Flying Physicians Association National Headquarters, P. O. Box 3275, Tulsa, Okla.

Inter-Society Cytology Council, Palmer House, Chicago, Sept. 23-25. Dr. Paul A. Younge, 1101 Beacon St., Brookline 46, Mass., Secretary.

Kentucky State Medical Association, Louisville, Sept. 20-22. Mr. J. P. Sanford, 1169 Eastern Parkway, Louisville 17, Ky., Executive Secretary.

Maryland, Medical and Chirurgical Faculty of the State of, Semiannual Meeting, Ocean City, Sept. 16. Mr. John Sargeant, 1211 Cathedral St., Baltimore 1, Executive Secretary.

Michigan State Medical Society, Detroit, week of Sept. 25. Dr. D. Bruce Wiley, 606 Townsend St., Lansing 15, Mich., Secretary.

Montana Medical Association, Baxter Hotel, Bozeman, Sept. 15-17. Dr. William E. Harris, 114 N. Second, Livingston, Montana, Secretary.

National Cancer Conference, American Cancer Society, Inc., and the National Cancer Institute, Minneapolis, Minnesota, Sept. 13-15. Dr. Roald M. Grant, 521 W. 57th St., New York 19, Coordinator.

National Recreation Congress, Shoreham Hotel, Washington, D. C., Sept. 25-29. Willard B. Stone, 8 W. Eighth St., New York 11, Secretary.

Nevada State Medical Association, Stardust Hotel, Las Vegas, Sept. 7-10. Mr. Nelson B. Neff, P. O. Box 2790, Reno, Nev., Executive Secretary.

New England Society of Anesthesiologists, Bretton Woods, N. H., Sept. 18-19. Dr. Thomas K. Burnap, P. O. Box 81, Kenmore Station P. O., Boston 15.

Oregon State Medical Society, Portland, Sept. 7-9. Mr. Roscoe K. Miller, 2164 S. W. Park Place, Portland 5, Ore., Executive Secretary.

Pacific Dermatologic Association, Empress Hotel, Victoria, British Columbia, Canada, Sept. 1-4. Dr. Edward J. Ringrose, 2636 Telegraph Ave., Berkeley 4, Calif., Secretary-Treasurer.

Society for Pediatric Radiology, Ambassador Hotel, Atlantic City, N. J., Sept. 26. Dr. Richard G. Lester, 412 Union St., S. E., Minneapolis 14, Minn., Secretary-Treasurer.

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